THE MEDICAL JOURNAL OF AUSTRALIA

VOL. II.—40TH YEAR SYDNEY, SATURDAY, DECEMBER 5, 1953 No. 23

Table of Contents.

[The Whole of the Literary Matter in THE MEDICAL JOURNAL OF AUSTRALIA is Copyright.]

ORIGINAL ARTICLES— Page.

Mathison Memorial Lectures—Virology as an Independent Science, by F. M. Burnet, M.D., F.R.S. 841
Some Remarks on the "Compensation Inguinal Hernia", by Thomas F. Rose, M.B., M.S., F.R.C.S., F.R.A.C.S., F.A.C.S., F.I.C.S. 845
The Analeptic Effect of Succinate in Coma and in Confusional States, by E. M. Trautner, E. R. Trethewie and S. Gershon 848
The Mortality in Australia from Cancers of the Respiratory System, by H. O. Lancaster 855

REPORTS OF CASES—

Infection with a Variety of Salmonella Choleræ-Suis, by David G. Failes and Charles E. Marshall 857
An Interesting Case of Hydatid Disease, by V. R. Harbison 858
Transfixion of the Eyeball with Recovery, by T. Boyd Law 858

REVIEWS—

Practice of Psychiatry 859
Medical Electricity for Massage Students 859
Operative Gynecology 859
Australia in the War of 1939-1945: Series Four (Civil); Volume I: The Government and the People, 1939-1941 860
Tumors of Bone: A Roentgenographic Atlas 860
Current Therapy, 1953 860
The Science and Practice of Surgery 860
Principles of Thoracic Anæsthesia 861
Gifford's Textbook of Ophthalmology 861
Pulmonary Tuberculosis 861
Textbook of Virology 861
Handbook of Orthopædic Surgery 862

NOTES ON BOOKS, CURRENT JOURNALS AND NEW APPLIANCES—

Family Doctor 862

BOOKS RECEIVED 862

LEADING ARTICLES—

Genius 863

CURRENT COMMENT— Page.

The Evolution of Child Care 864
Psychiatric Aspects of Asthma 865
Chronic Bronchitis and Antibiotics 866
Tuberculosis in South Australia 867

ABSTRACTS FROM MEDICAL LITERATURE—

Medicine 868

SPECIAL ARTICLES FOR THE CLINICIAN—

XC. The Management of Bladder Neck Obstruction .. 870

OUT OF THE PAST 871

SPECIAL CORRESPONDENCE—

London Letter 871

CORRESPONDENCE—

Comfort in Callipers 872
The Capacity of the Medical Profession in Australia to Absorb New Members 872
Folic Acid and Reproductive Efficiency 873
A Report on an Investigation of a Country Midwifery Practice, with the Preliminary Results of 300 Cases following Improved Obstetrical Care 873

OBITUARY—

James Hannibal Young 874
Jessie Strahorn Freeman 874

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA 875

MEDICAL PRACTICE—

Police Offences Amendment Act, 1908, as Amended 875

AUSTRALASIAN MEDICAL PUBLISHING COMPANY, LIMITED—

Annual Meeting 876

DEATHS 876

DIARY FOR THE MONTH 876

MEDICAL APPOINTMENTS: IMPORTANT NOTICE .. 876

EDITORIAL NOTICES 876

Mathison Memorial Lectures.[1]

VIROLOGY AS AN INDEPENDENT SCIENCE.

By F. M. BURNET, M.D., F.R.S.,

Walter and Eliza Hall Institute of Medical Research, and Department of Experimental Medicine, University of Melbourne.

LECTURE II: THE SUBSTANCE OF VIROLOGY.

In the preceding lecture I discussed the origins of virology as a response to the urgent human need of protection against small-pox and other serious diseases. But no collection of useful knowledge can be regarded as a science until it has been sorted into a logical and self-consistent sequence and shown in its general relationship to the broader fields of knowledge. Tonight I want to discuss virology as an existent science—its generalizations, its working hypotheses and, in particular, its relation at every point to one or other aspect of general biological theory.

When one can define the subject matter of a branch of biological science it is safe to assume that out of many people's ideas and discussions useful generalizations have begun to emerge.

Viruses are defined as microorganisms, potentially capable of producing disease, which are smaller than bacteria—the upper level being about 0·4μ for the largest dimension—and are capable of growth only within the substance of living cells of a susceptible host.

Virology as a science can be regarded essentially as the unfolding of the implications of that definition. The most important section is the second—the limitation of growth to the interior of the host cell. The small size is of secondary importance and is there to exclude the rickettsiæ from the definition. It would be quite logical to include rickettsiæ, but most microbiologists feel that both rickettsiæ and the intracellular protozoa are better kept in separate groups. However, no one has provided a satisfactory criterion for demarcating these two groups from the viruses, apart from the empirical one that morphological characters can be observed with an optical microscope. My own prediction is that eventually there will be added to the definition some statement that a virus multiplies within the cell by a process in which its individuality disappears for a time, to engender a "matrix" out of which new infective particles eventually develop. A gonococcus becomes an intracellular parasite of the leucocyte that engulfs it; but by microscopic observation, and in principle at least by culture of the leucocyte suitably disintegrated, it can be shown that multiplication is by binary fission. At every stage there are viable individuals.

[1] Delivered on October 7 and 9, 1953, at the University of Melbourne.

When a typical virus like that of vaccinia or of influenza enters a susceptible cell, there is a short period when by one means or another its existence can be detected. Then it disappears. There is an eclipse phase during which nothing detectable as a virus particle exists; but during this period a situation is being developed in the cell from which, after an appropriate time, a new brood of virus particles will rapidly come into being (Figure I).

This is characteristic of all viruses which have been adequately studied—a very small minority of them by the way—and introduces the necessity to consider any virus as a species with two phases in its life cycle. It can exist in the form of "infective particles", "elementary bodies" or "virus" in the ordinary usage of the term, but it also exists as a process so intimately bound up with the processes of its host cell that we cannot recognize the existence of the virus except by its potentiality of bringing forth at the due time a flush of new infective virus. This unindividualized phase may best be termed the multiplying phase, as contrasted with the infective phase of the virus species.

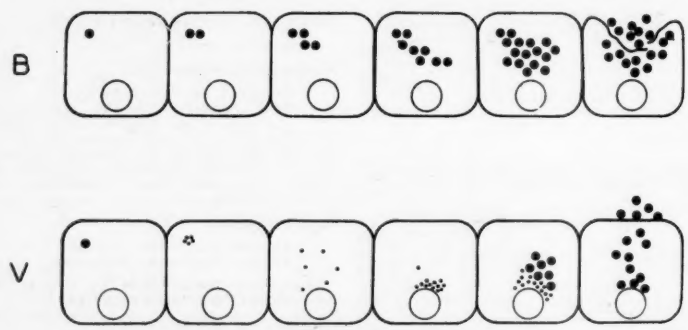


FIGURE I.

A diagram to illustrate the difference between intracellular multiplication of a bacterium (B) and a virus (V). Bacterial multiplication is by binary fission, virus multiplication by the development of a matrix from which the new generation of virus particles develops.

So much for our definition of a virus. To go farther into academic virology we have the choice of two paths—the way of the bacteriophages or the way of the influenza viruses. Ten years ago it was a well-known jibe that academic geneticists could be divided into two groups, those who worked with the fruit fly *Drosophila* and those who were interested in maize. At the present time there is a similar dichotomy amongst virologists. The most popular field is that of the bacterial viruses, the bacteriophages—a large group of viruses, members of which can parasitize bacteria of almost every type. There are many special virtues of the bacterial viruses that make them particularly suitable for study, and during the decade between 1927 and 1937 I was an enthusiastic worker in that field. But in 1935 I isolated the first Australian strain of influenza virus, and after that my allegiance swung rapidly over to the rival field—so much so that since 1940 virtually all my own work has been on one or other aspect of influenza virus. Many other investigators in England, in the United States and in the Netherlands have also found absorbing interest in the academic study of the influenza viruses. I shall therefore discuss the principles of virology from the standpoint of what is known about influenza viruses. It is a more difficult technical field than the bacteriophages and in some respects not so well developed. However, its great advantage from my present point of view is that influenza has high medical and human interest. Sometimes workers on bacteriophage tend to look up from the fascination of their researches and wonder with a faint sense of guilt what contribution they are making to the satisfaction of human needs or desires. Their answer is that eventually knowledge gained about bacteriophages may become useful or relevant for the prevention of human virus diseases like small-pox, poliomyelitis and influenza. Sometimes I have the same niggling sense of guilt in regard to much of our work on influenza viruses—it may never have much bearing on human affairs. Yet we cannot forget that three virus diseases—small-pox, yellow fever and influenza—have changed the course of human history in the past, that another virus disease, myxomatosis, may have added £50 million to the Australian national income last year, and that in the civilized and over-populated world of the "next million years" respiratory infections like influenza are likely to be the most important manifestation of infectious disease. I hope that most people will agree that the effective fundamental study of an agent so significant to medicine is an activity at least as justifiable as most other human occupations.

I shall take, then, influenza virus as the central model around which a general picture of the behaviour of viruses pathogenic to man and animals can be built. We shall have to study virus activities at several levels. There is, first, the nature of the infective particles that we normally speak of as virus, and second, the interaction of the virus and the susceptible cell, which culminates in virus multiplication and release. At the next level we are concerned with the pathogenesis of virus disease, how the virus spreads from its site of initial infection, and what determines the symptoms and the outcome of the infection. The fourth level is concerned with epidemiological aspects of virus disease; if we are thinking biologically, it is perhaps better to speak of the ecological level and think essentially of the interaction of two species, man and the influenza virus. Such a point of view allows an easy transition to the fifth and highest level, the evolution of the virus and the play of mutation and selective survival that controls this.

The Infective Virus Particle.

If we take the influenza virus and one of the pox viruses such as vaccinia and make purified and concentrated suspensions, we find in each case that the virus is made up of fairly uniform particles of characteristic size and shape in electron micrographs. A well-adapted strain of influenza virus gives roughly spherical particles about 100mμ in diameter, about one-tenth the diameter of an average coccus. More recently isolated strains tend to have a high proportion of filamentous forms, sometimes with a length of several microns and easily visible by ordinary dark-ground illumination. Vaccinia virus is much larger and of rounded rectangular shape, with a central condensation that may have some of the qualities of a nucleus.

Chemical studies of purified viruses show that they are composed of the same sorts of material as bacteria or animal cells. Vaccinia virus has protein, nucleic acid (both DNA and RNA), lipid and carbohydrate. Influenza virus is generally similar, but contains more lipid and probably has no DNA.

We shall be concerned most with influenza virus, and there are some functional qualities of the influenza virus particle that should be mentioned here. The particles which are present in thousands of millions in one of the allantoic fluids, and which we ordinarily speak of as virus, are infective particles, and to fulfil their function of transferring infection from one cell to another, they carry on their surface specially organized molecules that are there to make specific union with receptors of the cell surface and allow entry into the cell. They are also the agents against which immunity is directed, and on the surface of each virus particle there are the antigenic components which can stimulate the production of and react with the antibody that the body develops after an attack of influenza. It is a general rule that on the surface of the infective particle of any virus there are on the one hand the molecular groupings needed for its entry into the cell, and on the other the antigens which will allow the infected individual to become immune against a subsequent attack.

The Virus Cell Interaction.

Viruses by definition multiply only within living cells. It can be shown that under suitable conditions an influenza virus particle becomes attached to the surface of a susceptible cell, and that from three hours onward from the time infection was initiated, virus particles of a new generation begin to be liberated into the fluid bathing the cell. Something of the order of 100 descendant particles are produced, and in the process the cell may or may not suffer damage which is later manifested as vacuolation and necrosis. Twenty years ago we should probably have considered that having said that, there was little more to be sought for. In those days, when a cell multiplied it took in nutrients, enlarged, and at a certain stage divided into two. This process of binary fission was the fundamental means by which microorganisms multiplied, and there was little to be gained by trying to develop a deeper understanding of the process. It was known that some organisms were more demanding in their requirements than others, the pneumococcus required a more complex medium for growth than *Bacterium coli*, while viruses were satisfied with nothing less than the whole range of nutrients present in the cytoplasm of the host cell. With the general development of biochemistry this attitude began to change and we are now at the stage of trying to understand some of the processes that underlie reproduction. Up to the present the effort has not met with any outstanding success; but there is a curious sense of hopefulness amongst the biochemists that it is by the closer study of viruses and their action on the host cell that a real understanding of the process of growth and multiplication will be obtained. It is already clear that viruses like influenza do not multiply by binary fission.

In my description of the virus cell interaction I shall have to be dogmatic and state what I believe to be the best interpretation of the experimental facts without describing either the facts or the reasons for the interpretation. The first phase of adsorption of the virus to the cell surface has been the object of seven years' study by our own people at the institute, but I shall have to condense their findings into a single paragraph.

The influenza virus enters the cell by undergoing specific adsorption to mucoprotein molecules that form a meshwork over the free surface of the respiratory epithelium or other type of susceptible cell. The virus carries on its surface certain molecular groupings which attach to complementary grouping on the mucoprotein. Once firmly attached, the virus particle sinks into the cytoplasm. There is a second phase of the action of the virus on these mucoprotein receptors—their destruction by enzymatic action. The biological function of this striking enzymatic activity is still obscure, but it appears to have no significant part to play in the entry of the virus into the cell.

To understand what happens when the virus particle enters the cell, we have to think of its structure in a different way from the chemical approach we adopted previously. You remember the nineteenth century differentiation of the germplasm from the soma, and the paradox that the essential continuing part of a species was the genetic mechanism carried in the germ cells, and that the body, the soma, was to be thought of merely as the machinery needed to protect, to nourish and to pass on the genetic pattern. In much the same way one can think of a virus particle as composed of somatic and genetic parts, the soma and the genome. The surface characters of the virus, its immunological nature, its adsorptive hæmagglutinating and enzyme-like activities are somatic, and they are the only static qualities by which the existence of virus can be recognized. The genome has as yet no detectable qualities by which its presence can be recognized, short of testing the power of the virus to multiply. The possibility that its physical basis is the 1% of nucleic acid (almost wholly RNA) present in the virus particle is likely enough but has not been established.

The virus becomes undetectable soon after it enters the cell, and we must assume that somatic material disintegrates and plays no further part in the process. In the basis of what has been found out about bacterial viruses, the genetic material is presumed to be the only part of the virus particle that initiates the process of multiplication.

Virus genetics is a very new subject, and to date the only published work on the experimental study of influenza virus genetics comes from the Walter and Eliza Hall Institute. The rest of the world has as yet expressed no opinion; but I am hopeful that the development of methods for studying the genetics of viruses pathogenic for animals may come to be regarded as the most important contribution the institute has made to microbiology. What I have to say on the matter is therefore unconfirmed by other laboratories. It will certainly have to be modified when overseas workers attack the same problem with different backgrounds and different technical approaches. Our current interpretation of the genetic structure of influenza virus A is a provisional one, and even if it should turn out to be correct, it by no means follows that it can be taken as a pattern for other viruses. We believe that each virus particle contains two (and perhaps sometimes more than two) complete genetic units (genomes), and that each genome is composed of two linkage groups, each analogous as it were to a chromosome in higher forms. When a virus particle breaks down within the cell, each linkage group is set free to find its own opportunity for multiplication. No one really knows how new virus is produced, just as no one knows how any form of biological pattern in gene, antigen or enzyme is replicated in the cell; but there is very general agreement that in some way or other the virus genes, perhaps in the form of two strings of linked genes, take over the control of much of the synthetic activity of the cell. The cell is forced to provide the atoms and the energy needed first to replicate the pattern of the linkage groups, and either subsequently or concurrently to construct the molecules that will be needed for the soma of the virus particles that will eventually emerge. There must be some little miracles of organization to bring that to pass; but they are miracles of the same quality as those being performed every second in every cell of every living organism. It is in fact from the intrusion of the virus into such mechanisms that we draw our best hope of learning something about them.

The essentials for a group of virus particles are eventually assembled, the pieces for one come together and fall into the necessary relation one to another. There is much to suggest that the final organization takes place in that part of the surface layer of the cell through which the newly formed virus particle will escape to the environment. It may be that while passing through the surface layer the virus picks up the lipid and polysaccharide molecules which are regularly found in analyses. Some have suggested that the influenza virus is no more than a fragment of cell cytoplasm stamped with a series of alien patterns. One cannot really quarrel with this assertion; but after all the only real differences between organisms can be related much more to differences in pattern than to differences in material. It is self-evident that more than 99% of atoms in a new brood of influenza particles have come from the host cell, and it is only to be expected that some of the molecules incorporated may still carry antigenic patterns, recognizably of the host, whenever such a pattern does not interfere with the function of the virus as virus.

In other viruses, notably those responsible for the pox diseases, the process of multiplication appears to be more precisely organized than that of influenza virus; but equally here we have an apparent accumulation of components into a stock-pile before the new generation of virus particles begins to emerge.

As the new particles of influenza virus emerge, they tend to accumulate on the free surface of the cell until they are liberated from their attachment by their own enzymatic action. Once free, they are available to continue the process by initiating infection in adjacent cells.

Pathogenesis.

This brings us to the next level of virus activity—the movement and multiplication of virus within the body as a whole, the pathogenesis of virus disease. Here we shall find it valuable to continue to keep in mind our central concept of the virus and the susceptible cell. Virus disease

must always commence by the initiation of infection in one cell or in a few single cells. Multiplication will be followed by liberation of virus and its transport by one means or another to other susceptible cells. The character of any virus disease is determined by the range of susceptible cells, by the mode in which virus is liberated from the infected cells, and by the opportunities for transport through the body.

I can mention only two examples from human disease, small-pox and influenza. Both have been studied in detail with strains of virus adapted to produce a broadly analogous disease in the mouse. The most important studies in each case have been carried out in the institute, those on mouse-pox by Fenner, those on mouse-adapted influenza virus by Fazekas. The initial infection in small-pox is unknown, but in mouse-pox it takes place through some minor abrasion of the skin. The pox viruses have highest affinity for the deeper-living cells of the skin epidermis, but they can also multiply freely in a wide variety of epithelial and mesenchymal cells. They can multiply in lymph nodes and leak over into the blood. In the case of mouse-pox, the most important process going on in the incubation period is a sequence of spread and multiplication to local lymph nodes to blood, with transport to liver and spleen where major multiplication occurs and gives rise to a secondary viræmia that is responsible for widespread infection of the skin. This is finally manifested as the generalized rash which is the mouse's equivalent of the small-pox rash in man. I do not think that small-pox and measles follow quite this pattern in man; but I am confident that, broadly speaking, mouse-pox is the best experimental model yet provided for the human exanthemata.

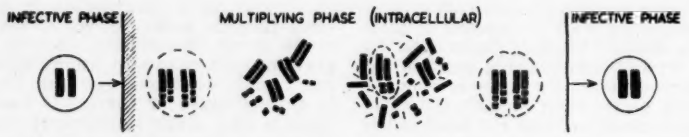


FIGURE II.

A diagram based on recombination experiments with influenza viruses to give some idea of the behaviour of the genetic material during intracellular multiplication. The essential features are the independent replication of linkage groups and the subsequent reconstruction of infective virus particles.

Influenza virus differs primarily in the fact that it can multiply freely only in the respiratory epithelium and is characteristically liberated on the superficial surface of the cell it infects. Initial infection almost certainly takes place in the lining of one of the smaller bronchioles, and the first liberation of virus is onto the surface of the cell, where the particles diffuse or are moved by ciliary action in the film of moisture that overlies the respiratory mucosa. Spread is therefore surface spread and eventually involves a large portion of the bronchiolar epithelium. It is the general belief that normal influenza does no significant damage elsewhere. However, post-mortem findings in 1918-1919 influenza pointed to an intense attack on the epithelium above and below the bronchiolar level. Necrosis of tracheal and bronchial epithelium was described, as well as an alveolitis which was probably a direct effect of the virus.

When the respiratory epithelium is under attack a proportion of virus and virus products passes into the lymph vessels and reaches the lymph nodes. There is no evidence whether virus reaches the blood, but if it does, it never produces metastatic lesions. It takes an enormous dose of virus given intravenously to produce lesions in the mouse lung, and no multiplication in other organs has been detected.

I have no time to discuss the spread of other viruses within the body, but in each case the same principles can be applied. The sequence is always determined by the distribution of cells susceptible to virus attack and the anatomical pathways by which they can be reached from the site of initial infection.

The Survival of a Virus in Nature.

Epidemiology is merely a limited approach to part of the broader topic of ecology—the science dealing with the interaction of species and individuals with their environment, and especially in relation to the other organisms, plant and animal, of that environment. In every epidemiological-ecological problem there is one key question to be answered: How does the virus survive from case to case, from epidemic to epidemic, and from century to century? If we can answer that question fully, we can almost always say at once whether the disease can be prevented and at what point in the process the most effective action can be taken. When we cannot answer the question, we can hardly ever attempt rational measures of prevention; serum hepatitis is the outstanding example.

For most virus diseases there is one characteristic of overriding epidemiological importance—the development of immunity. Virtually no one has small-pox or measles a second time, and in what we may regard as standard virus diseases this long-lasting immunity against the type of virus causing the first infection is characteristic. To survive, each virus has to find its own way of circumventing this situation. When a virus can pass freely through the community by contact it is obvious that if it immunizes all those it attacks, cases will be confined to the younger age groups, and—a very useful rule — the more freely the virus can spread, the younger will be the average age of clinical infection. A disease like measles or chicken-pox appears to spread in perfectly straightforward fashion by droplet spread of infected saliva from patient to susceptible child. The infection is always moving somewhere and sooner or later will always return to any area in which a new population of susceptible children grows up.

Influenza provides an interesting variant from this behaviour. There is much to suggest that an attack of influenza provides on the average a much longer lasting immunity against the same sort of influenza than is usually believed. Influenza A and probably also influenza B have developed a counter to this immunity which enables them to pass periodically through adults as well as children. This is a phenomenon which may be called "immunological drift". The virus is mutable, and probably minor serological variants are always arising. The further a virus changes from the serological pattern of the virus responsible for the last major epidemic, the more likely it will be able to pass through a partially immune population. So we find a steady drift toward serological novelty in successive types of influenza A virus. At intervals the difference becomes so great from the last type strain in the laboratories that we speak of the emergence of a new type. However, everything points to changes occurring as an irregular drift and not by a series of large discontinuous leaps. No other instance of this "immunological drift" has been detected; but an examination of the record of dengue epidemics makes me feel very confident that future work will show the process at work here also.

With the rarer virus diseases, immunity is of no importance, incidence being determined essentially by the existence of opportunity for infection. More orthodox ecological factors may play the major role. The story of Australian X disease and Murray Valley encephalitis, as worked out by Anderson and his colleagues, provides a particularly interesting picture of the interplay of vector, reservoir, weather and environment. Encephalitis enters the Murray-Darling basin only at irregular intervals—1917, 1918, 1925 and 1951. It persists in some reservoir in the tropics, perhaps in northern Australia, perhaps in Indonesia. Only in those years with an excessive southward spread of early summer rainfall do the conditions become appropriate for the virus to move south. It passes from bird to bird by the bite of culicine mosquitoes, and we can imagine that a bird infected in the north may travel 100 or 200 miles south before the virus develops sufficiently in

its blood to infect another mosquito. Only when there is a more or less unbroken staging route for the virus from the tropics to the south can it reach the Murray. When it reached Mildura in 1951, it spread very widely during the summer and autumn. With plenty of mosquitoes and plenty of nestling water birds there was every opportunity for infection to be carried to any bird or mammal, including man, on which *Culex annulirostris* would feed. But when that mosquito vanished with the onset of winter, the virus found no opportunity for local survival and disappeared. In the two following summers, despite intensive efforts, no evidence of the existence of encephalitis virus in southern Australia has been obtained.

For every well-studied virus disease there is an equally interesting tale to be told of how the virus finds it possible somewhere to persist indefinitely and in other places or circumstances to appear only as a transient visitor. As in the case of Murray Valley encephalitis, man may have no real significance in the cycle or, as in measles, he may be the only species concerned.

The Evolution of Viruses.

Viruses are organisms—no one has any doubt about that today—and each form must have an evolutionary history. We cannot expect to find fossil evidence of viruses, and any discussion of their evolution is necessarily largely speculative. I think that most virologists favour the hypothesis of parasitic degeneration from larger pathogens, some from bacteria, some perhaps from protozoa. There is no lack of intermediates. Take a typical rickettsia like that responsible for "Q" fever. It has a very close and curious resemblance on the one hand to *Brucella abortus*, a normal enough bacterium, and on the other to psittacosis virus. The behaviour in the mosquito of viruses like those of yellow fever and Murray Valley encephalitis is in many ways very similar to that of the malarial parasites, and it does not seem too fantastic to believe that they may be diminished descendants of some mosquito-borne protozoon. What I have said about influenza will indicate that the evolution of the viruses is still continuing. New diseases have appeared from time to time and old diseases have taken on new forms or new intensities, and we can probably expect an occasional unpleasant surprise in the future.

This very abbreviated account will, I hope, give you some idea of the substance of virology at the various levels. At each level the phenomena with which we are concerned in virology can be brought into relationship with more general biological phenomena at the same levels of organization.

I should like to stress particularly the contribution that virus research can make to general biology, and I do not think that I can do it better than by giving you a very brief account of two major developments in last year's work on influenza virus at the institute.

I mentioned earlier the way an influenza virus attaches itself to mucoprotein on the cell surface. The details of that action have been under study by Dr. Gottschalk for some years, and his work has culminated this year in the isolation of a new amino acid (pyrrole 2 carboxylic acid) which, in addition to being the key point of virus attachment, is probably of much wider general significance as the standard intermediary group by which carbohydrate components are integrated into the structure of complex proteins. This is work of the highest significance—I know of no more important single contribution to biochemistry from Australia.

The second development comes from a group of my colleagues that is working on influenza virus genetics. Their current work is opening up another field which may lead to significant advances in the understanding of virulence. In a number of instances, when two strains of widely differing virulence are allowed to infect the same cell, the descendant virus types obtained show many of intermediate virulence. Virulence is apparently determined by the quantitative distribution of certain genetic units. From the human point of view almost the only thing that matters about a virus is its virulence. To immunize against yellow fever we want a virus of much lower virulence than normal, but otherwise of the same general structure. To destroy rabbits we need myxomatosis virus of maximal virulence, and we feel disappointed when natural processes in the field lead to a reduction of virulence. This indication from our present work that there is a quantitative genetic basis for virulence may also have important repercussions on general genetic theory, particularly as it applies to micro-organisms.

Conclusion.

Science has no limits. Our brains and minds being of the same stuff as the phenomena that they try to comprehend can have no hope of final answer. The complexity of things, and above all the complexity of living things, will always defy comprehension within a simple logical pattern. Nor is it likely that the accumulation of systematic knowledge arranged and made accessible by the best of the new machines for storing and handling information will ever even provide all that is needed for dealing with the ever-changing practical problems of medicine and agriculture. Theoretical and practical biological research can provide perennial fascination for scientists of future centuries as well as for our own generation.

If Mathison had been alive today he would be aged nearly seventy years, and he would have seen a great change in the nature of medical research since the days of his apprenticeship and early work. But now, as then, he would still see the essential association of fundamental biology with practical medicine. I like to think that he would agree with me that there are two rules for every medical research worker who aspires to greatness. The first: no matter how immediate and practical the problem that is being studied, look at its significance from the point of view of each of those wider levels of medicine and biology for which it is inevitably significant. The second: retain your faith that there is no aspect of fundamental research in biology that may not one day be relevant to the advance of medicine and the future of the human species.

SOME REMARKS ON THE "COMPENSATION INGUINAL HERNIA".

By THOMAS F. ROSE, M.B., M.S. (Sydney), F.R.C.S. (England), F.R.C.S. (Edinburgh), F.R.A.C.S., F.A.C.S., F.I.C.S.,

Consulting Surgeon, Hornsby and District Hospital; Honorary Surgeon, The Royal North Shore Hospital of Sydney; Relieving Surgeon, Department of Repatriation, Sydney; Tutor in Surgery, The University of Sydney.

THE purpose of this article is to examine some aspects of the inguinal hernia incurred at work. Since a patient with such a hernia is entitled to compensation, its cause must be carefully verified by the examining surgeon.

The Criteria of an Inguinal Hernia Incurred at Work.

What criteria should be used to determine whether or not an inguinal hernia has been incurred at work? It has been stated that for a claimant to receive compensation for such a hernia the following criteria must all be satisfied: (i) There must be a history of effort unusual for the patient immediately preceding the onset of the hernia. (ii) Immediate pain and tenderness in the affected area must be present. (iii) Nausea or vomiting must occur. (iv) The patient must be unable to carry on his work, even if only for a short time. (v) An immediate painful and tender swelling must appear in the affected groin. (vi) At operation, in a recent case, the hernial sac must be thin-walled with no adhesions either in or surrounding it.

To test the validity of this assertion, using these criteria, I have analysed the histories of 71 patients with inguinal

hernia incurred at work[1] who were successful in their bid for compensation.[2] All were males, and their ages ranged from sixteen to seventy-five years.

When the criteria were examined *seriatim* the following results were found:

1. All 71 patients attributed the onset of their hernia to some effort at work—as, for instance, lifting heavy weights, pushing trucks, pulling levers *et cetera*. In only 32 cases was the effort unusual, and in 22 of these this was because it was associated with the patient's simultaneously slipping or falling. The consequent attempt to save himself and his load caused a greater rise in intraabdominal pressure than would otherwise be expected. In the other 10 cases the patients' normal occupation was clerical, but they were helping at unaccustomed harder work. In the remaining 39 cases the effort, though great, was not an unusual one. In each case the incident causing the hernia was witnessed or reported immediately to the correct authorities.

2. In every instance immediate pain and tenderness were both present in the affected groin. In 67 of the cases the pain was severe and sharp, stabbing or tearing in character. In the other four it was of less intensity and was aching or throbbing in character. One man felt "something slip" with the sharp pain. In four cases the groin pain was also accompanied by generalized abdominal pain. Naturally such a subjective symptom as pain is difficult to evaluate, one having to rely on the patient's description of its type and severity. Some patients are more phlegmatic than others and seem to suffer less pain than might be expected.

3. In no instance did any of these patients vomit, and in only 24 was there any nausea.

4. Thirty-eight patients did not cease work for an instant. Eighteen ceased work for five minutes or less, ten for half an hour, two for an hour, one for one day, one for one week and one for two weeks. The two last mentioned did so on medical advice, the others because of the pain.

5. The swelling caused by the hernia appeared at variable times after the incident causing it. In 14 cases only did the swelling appear immediately or within a few minutes. In nine it appeared within an hour, in 16 in from one to twelve hours, in 19 in from twelve to forty-eight hours, in 10 in from two to seven days, and in three in from two to five weeks. Between the onset of the pain and the appearance of the hernia the affected groin was painful and tender, although usually not so intensely as when the accident occurred. All the swellings were painful and tender when first noticed by the patients, and these manifestations lasted a variable length of time, in some as little as three weeks and in others as long as six months.

6. Only 28 of the 71 patients were operated on before their claims were settled. All of these had hernias of recent onset, 21 within a few weeks, the rest up to two years. In each instance the sac of the hernia was thin-walled and there were no intrasaccular or perisaccular adhesions. (No patient had worn a truss, which is a well-known cause of a thick-walled sac with adhesions.)

The foregoing findings may be summarized as follows. All these patients had an unequivocal history of effort, not necessarily unusual, causing the hernia. Pain and tenderness in the affected groin occurred immediately at the time of the effort. No patient vomited and only one-third experienced nausea, whilst less than half of them found it necessary to cease work, and then mostly for only a short time. The hernial swelling appeared at varying intervals from instantly to five weeks after the incident. In the interim the affected groin was painful and tender, as was the swelling when it appeared.

[1] There were actually 74 consecutive hernia cases, the other three consisting of a femoral, a paraumbilical and an epigastric hernia. This is mentioned to show the relative frequency of the different types of compensation hernias.

[2] These patients were awarded compensation, by immediate acceptance of their claim by the respective insurance companies, or by their case being settled out of court, or by their winning it in the Workers' Compensation Court.

Grounds for a Successful Bid for Compensation.

From the foregoing analysis it is shown that certain findings must be present in order to establish a claim for compensation for these hernias.

The history of the incident causing the hernia is one of the most important pillars on which the patient's claim rests. An uncertain or equivocal history, especially if the incident is not witnessed or reported immediately, spells the doom of the patient's hopes in court. A prior history of chronic cough, difficult micturition or straining at stool, none of which the patients in this series had, will raise doubts as to the genuineness of the claim.

Pain and tenderness must immediately occur with the effort allegedly causing the hernia. This fact is a *sine qua non* of success in winning compensation.

The patient need not vomit, feel nauseated or lose work, since these phenomena depend not only on the severity of the injury, but also on the patient's fortitude.

The appearance of the swelling need not be immediate, *but it must be painful and tender when it does appear.* Pending its appearance, the affected inguinal region must be painful and tender.

When operative findings are available before the claim is heard in court, the sac of a recent hernia must be thin-walled and there must be no adhesions (provided a truss has not been worn).

Causes of Failure in a Claim for Compensation.

The following points will definitely prevent a claim from being won, because it is obvious that such a hernia could not have been due to the incident alleged.

1. A vague uncertain history, especially if unsubstantiated by a reliable witness, or if the incident is not reported as soon as practicable. A patient who steps off a motor-lorry running-board as he has done many times a day for many years, can hardly expect this act to be believed to be the cause of a hernia. A blow on the groin by itself, even severe enough to cause a bruise, is not enough to cause a hernia; it must be accompanied by a sudden rise in intraabdominal pressure as well.

2. A pain-free interval separating the incident allegedly causing the hernia from the onset of groin pain and tenderness.

3. The absence of pain and tenderness in the swelling of the hernia on its initial appearance at least.

4. At operation the finding of a thick-walled sac with adhesions. This is obviously not that of the recent hernia for which most claims are made, unless a truss has been worn for some time.

The Type of Inguinal Hernia Incurred at Work.

To what type of inguinal hernia does the work-incurred hernia belong? Is the hernial sac direct or indirect? This is a very pertinent question in a series such as this, because, whilst one usually expects about 18% of direct hernias in a routine hospital series of inguinal hernias due to all causes in males in this age group (sixteen to seventy-five years), here 11 of the 28 hernias operated on were direct. This is twice the usual occurrence, a finding obviously due to the fact that effort was the cause of each of these hernias.

The differentiation between the direct and indirect inguinal hernias is important, because, while no one denies that the sac of a direct hernia (or of a recurrent inguinal hernia, whether direct or indirect) is acquired, there still seem to be doubts in the minds of many as to whether the sac of the adult indirect hernia incurred by effort at work is acquired or congenital. If one can say definitely that the hernia is acquired, one argument at least in favour of compensation is settled, whereas if one decides that the sac is congenital, then compensation may not be granted.

Consequently, the first step with any non-recurrent inguinal hernia said to be incurred at work is to determine whether it is direct or indirect. This can be done satisfactorily only at operation, because of the difficulty, even

impossibility, of pre-operative differentiation as exemplified below in this series.

The hernias of these 71 patients were subdivided as shown in Table I.

That it is hard to differentiate clinically the direct and indirect hernias may be realized because, of the 11 patients with a proven direct hernia, all but one (who had bilateral hernias) were diagnosed pre-operatively as having an indirect hernia. Consequently, of the 36 patients with a clinically indirect inguinal hernia yet to be operated on at the time of the settlement of their claims, 10 at least might have had a direct hernia.

Differentiation of these hernias may be made even more difficult because an indirect and a direct hernia may occur simultaneously on the same side, as occurred in four cases in this series.

To complicate the diagnosis of these hernias further, we now know, despite previous teachings to the contrary,

TABLE I.

Patients.	Type of Hernia.	Number of Cases.	Totals.
Patients who had not been operated on before settlement of their claim.	Clinically indirect inguinal hernia	36	43
	Clinically direct inguinal hernia	2	
	Recurrent clinically indirect inguinal hernia	5	
Patients on whom operation had been performed.	*Indirect inguinal hernia*	14	28
	Recurrent indirect inguinal hernia	3	
	Direct inguinal hernia	5	
	Direct *plus* indirect inguinal hernia on the same side	4	
	Bilateral direct inguinal hernia	2	
Totals			71

that a direct hernia may become complete and reach the bottom of the scrotum or may even be strangulated. (Two patients with the former and five with the latter types of direct hernia have been examined recently at the Royal North Shore Hospital of Sydney. Hogan and Rhoades (1953) saw no strangulated hernias in 219 cases of direct hernia.)

Age is no help in the differential diagnosis. In the 50 cases of indirect inguinal hernia, the ages of the patients ranged from sixteen to seventy-five years, the majority (42) being aged between thirty and sixty-nine years. The ages of those patients with a direct hernia ranged from thirty-three to forty-three years.

Consequently it is folly to argue before operation whether a hernia is congenital or acquired, because usually it is not known whether it is direct or indirect. Ideally, therefore, operative findings should be known before the merits of a hernia case are judged.

Is the Hernial Sac Congenital or Acquired?

It has often been said that, because an indirect inguinal hernial sac in an adult may appear immediately or within a few hours or days of the incident causing it, the sac must be congenital.

This statement is fallacious because, when the times of appearance of the indirect work-incurred inguinal hernias are compared with those of the obviously acquired direct and recurrent work-incurred hernias they are seen to be approximately the same. Of the 14 proven indirect hernias, two appeared immediately, four within two hours, three within twelve hours, two within two days, one in four days, one in seven days and one in ten days. In the 11 patients with the 13 proven direct hernias (two having bilateral hernias), two hernias appeared immediately the incident occurred, five appeared within two hours, one in twelve hours, four in two days and one in four days. (It is interesting to note that the bilateral hernias did not appear simultaneously, though of course in each instance both inguinal regions were immediately painful and tender. In one patient one hernia appeared in two hours, the other in two days. In the other patient one appeared immediately and the other in seven days.) In the eight patients with recurrent hernias, two hernias appeared immediately, one in five minutes, two in an hour, two in eight hours and one in two days.

An equally fallacious statement is that if an indirect hernia increases quickly in size, it must again be of congenital origin.

Nine of the 14 indirect hernias stayed as bubonoceles (even up to two years). Three reached the neck of the *scrotum, one in two weeks, one within a month and one in* three months. Two became complete, one reaching the bottom in two weeks and the other in four months. On the other hand, the obviously acquired hernias, the direct and the recurrent, increased just as quickly in size. Ten *of the 13 direct hernias remained as bubonoceles. The* other three reached the neck of the scrotum, two in one month and the other in three months. None became *complete. Five of the eight recurrent inguinal hernias remained* as bubonoceles. Two reached the neck of the scrotum, one within ten days and the other in five weeks. One became complete within two months.

Consequently the speed of appearance and increase in *size of all these hernias—indirect, direct and recurrent—* are more or less the same and cannot be used as an argument to say that a quickly appearing and rapidly growing indirect inguinal hernia must be of congenital origin.

It is agreed, of course, that many indirect inguinal *hernias first occurring in adults may be of congenital* origin. However, the history given by these patients differs significantly from that given by patients with work-incurred hernias, whose story of effort followed by pain is so characteristic.

These patients with congenital hernia all have a history of painless swelling with no history of effort. The records *were examined of 100 consecutive male patients admitted* to the Royal North Shore Hospital with indirect inguinal hernia, and in the same age group as the series presented here. This investigation showed that 62 patients noticed a painless swelling in the groin with no history of effort; in fact, four of them did not realize they had a hernia at all until it was demonstrated at an insurance examination. These hernias were obviously of congenital origin. The remaining 38 hernias were just as obviously acquired, the patients having a history of a painful swelling occurring *after pain in the groin due to effort at work (12 cases),* chronic cough (six cases), chronic constipation with straining at stool (one case), prostatic obstruction (three cases), and urethral stricture (one case). Thirteen hernias occurred after the patient had suffered from intermittent attacks of groin pain for many years. Two of the hernias were recurrent.

Thus it is obvious that there is a vast difference between the work-incurred indirect hernia and the congenital indirect hernia of adult life.

Pathology of the Work-incurred Hernia.

The pathology of these acquired, effort-caused indirect hernias is that the sudden rise of intraabdominal pressure forces, by means of a loop of bowel or a piece of omentum, a loose fold of parietal peritoneum (and anyone who operates in this region knows how loose the peritoneum can be here) as a diverticulum down the inguinal canal, suddenly dilating it. If a large process is pushed down, then the swelling may become apparent to the patient at once; if only a small process is pushed down, then it is concealed by the musculature of the anterior wall of the inguinal canal until it becomes larger. Once started, this peritoneal diverticulum is pushed down the canal by any further rises of intraabdominal pressure (such as occur in everyday life), being transferred to the sac by the hydrodynamic action of the contents. Each rise consequently drags more peritoneum from the abdominal wall into the inguinal canal. The pressure stimulus from its contents also causes an increase in size of the hernia by an increase in growth of the endothelial lining of the sac.

The same mechanism accounts for the direct and recurrent inguinal hernia and is the reason why all these inguinal hernias can appear and increase in size so rapidly, and why recent sacs are always thin-walled with no adhesions.

The pain and tenderness in the inguinal region are caused by the forcing apart of the walls of the inguinal canal by the hydrodynamic pressure of the sac contents. The dragging on the somatic peritoneum caused by the pushing out of the diverticulum is the reason for the abdominal pain which was experienced by four of the patients in this series.

These remarks are substantiated by a patient of mine (not in this series), on whom I was able to operate within eight hours of the injury causing the hernia.

This patient, aged thirty-five years, who had never had a hernia before, slipped while helping to lift a weight of 300 pounds and was seized immediately with severe pain in the left groin. He was nauseated and noticed an immediate painful and tender swelling in the groin. Examination disclosed a left inguinal bubonocele, which was so painful and tender that it was thought to contain strangulated bowel. At operation the cord was found to be very swollen and œdematous with some ecchymoses about the sac. The sac was indirect and thin-walled, and had no contents save for a little serous fluid. It extended down to the external ring, which was small in size, and there were petechial hæmorrhages scattered throughout its walls.

Another case, also not in this series, showed how quickly a sac can increase in size.

Opration was performed on a male patient, aged twenty-five years, who had a complete, indirect inguinal hernia of some years' duration which, as it had always been painless, was almost certainly of congenital origin. The sac was removed and a Bassini type repair was effected, stainless steel sutures being used. Unfortunately, convalescence was complicated by acute bronchitis with severe coughing, so that within fourteen days a recurrent hernia was entering the neck of the scrotum, pain having been felt in the groin from a week after operation. Operation three weeks later disclosed a thin-walled indirect sac entering the scrotum.

Consequently I believe that in these cases of work-incurred inguinal hernias the sacs are acquired and not congenital.

The Lax External Ring.

It has been suggested that a lax external ring is the outward revelation of a weakness in the inguinal canal predisposing to hernia. There is absolutely no proof of this, because the size of external rings varies in different individuals and indeed in the same individual without any hernia being present. Naturally, if a hernia is present and goes through the external ring, it will be enlarged.

Summary.

Seventy-one cases of inguinal hernia incurred at work in which compensation was successfully claimed are discussed.

It is shown that to establish a successful claim for compensation in such cases the cause must be attributed to a definite effort on the part of the patient, not necessarily unusual. Pain and tenderness in the affected groin must occur immediately after the injury. The patient need not vomit, be nauseated or stop his work. The swelling due to the hernia need not appear immediately after the incident, but the groin must be painful and tender until it does and the swelling must be painful and tender initially at least. If the hernia is recent, operation will show the sac to be thin-walled with no adhesions (the exception being if the patient has worn a truss).

It is asserted that in these work-incurred hernias the sac of the indirect hernia is acquired and not congenital.

Some of the reasons for the failure of a bid for compensation are discussed.

Reference.

HOGAN, W. H., and RHOADES, J. E. (1953), "Inguinal and Femoral Hernia", *Surg., Gynec. and Obst.*, 96: 226.

THE ANALEPTIC EFFECT OF SUCCINATE IN COMA AND IN CONFUSIONAL STATES.

By E. M. TRAUTNER and E. R. TRETHEWIE,
Department of Physiology, University of Melbourne,
AND
S. GERSHON,
Mental Hospital, Royal Park, Melbourne.

IN recent years the intravenous injection of high succinate concentrations has been recommended as an efficient antidote in barbiturate poisoning (Soskin and Traubenhaus, 1943, working on rats and dogs; Barrett, 1947 and later, working on man). The question is controversial. Lardy *et alii* (1944) and Carson *et alii* (1945) could not confirm any significant and beneficial effects on dogs, cats, rats and rabbits, and did not consider succinate to have any life-saving effect. Furchgott and Schorr (1948) pointed out that succinate in metabolic experiments conducted at low oxygen tension merely competed with the normal metabolism for oxygen without contributing any utilizable energy, and Wolfenberger (1948) showed that, in the presence of pentobarbital ("Nembutal"), succinate, while being itself oxidized at a high rate to fumarate, still further depressed the already lowered endogenous metabolism of heart muscle. Barrett (1949), however, reaffirmed his statement that there was an analeptic action of succinate in barbiturate poisoning and narcosis of man, and presented an impressive number of cases and observations to support his claim. The present investigation was conducted with the following purposes: (*a*) to establish whether any analeptic or other effect of succinate could be observed on barbiturate or other coma of animals or man; (*b*) to establish whether any stimulating or other effect of succinate could be observed on brain tissue respiring in the presence of barbiturate; and (*c*) if so, whether any indication could be presented as to its possible mode of action.

MATERIALS AND METHODS.

For animals succinate was used as a 30% solution of the hydrated sodium salt (about 1·1 normal or 18% solution of the anhydrous salt) in a dose of three millilitres per kilogram given intraperitoneally, intravenously or intracardially. In man, 5% to 10% solutions (anhydrous) were used intravenously; orally, one to four grammes per day were taken as tablets.

The barbiturate used in the animal experiments was "Nembutal" (pentobarbital sodium) in a dose ranging from LD_5 to LD_{90} given intraperitoneally. In man, thiopental, 0·5 to 0·7 gramme given intravenously, was used.

Respiration was recorded by means of pneumatic cuffs placed round the thorax and the abdomen and connected with a Marey tambour. Blood pressure was recorded through a cannula inserted into the carotid artery and connected with a mercury manometer.

The manometric observations were made by the Warburg technique, guinea-pig brain being used either in thin slices or as a mince prepared by passing the fresh, cleaned brain through a 60-mesh sieve. The conditions were as follows: a temperature of 37·5° C.; 100 shaking/minute; air; sodium hydroxide paper in the centrewall; Krebs phosphate Ringer solution; 100 to 150 milligrammes of tissue in four to five millilitres of fluid; pH 7·4. Oxygen uptakes are recorded as the values calculated for 100 milligrammes of tissue.

RESULTS.

Animal Experiments.

Animal experiments were conducted on guinea-pigs and rats, and on dogs and cats.

Guinea-pigs and Rats.

The animals, in batches of six to 12, were injected intraperitoneally with 25 to 75 milligrammes of "Nembutal" per kilogram, the highest dose being almost always fatal. Half the animals received, after a varying interval, three milli-

litres of 30% succinate solution per kilogram by intraperitoneal, intravenous or intracardial injection; the other half received at the same time the same amount of isotonic or hypertonic saline by the same route. Respiration and heart beat, muscular reactions, reflexes, rousability, and the duration of narcosis or the occurrence of death were noted.

Effect of Succinate on the Non-anæsthetized Animal.—The slow intracardial injection of succinate in the intact animal was performed in two guinea-pigs; no deleterious effect was evident. Both animals showed no signs other than temporary shock from the operation; a minute or two after the injection they were indistinguishable from normal animals in behaviour. Intravenous injection into the non-anæsthetized animal was not attempted. Intraperitoneal injection produced no noticeable effects.

Even high doses of succinate did not produce the excitatory, convulsive, or emetic effects exhibited by other analeptics, such as strychnine, picrotoxin, "Coramine", "Cardiazol", "Dexedrine" *et cetera* (compare Chakravarti, 1939).

Toxic Effects in the Animal under Barbiturate Narcosis.—A too rapid intravenous or intracardiac injection of succinate may cause cardiac arrest. This was usually of short duration, the heart resuming its action after a few seconds either spontaneously or on rhythmic compression of the thorax. Five of some 70 animals died during the intracardial injection. A transitory arrest of respiration was more frequently observed, usually followed by excessive deep inspirations. All surviving animals were perfectly well on the following day. No late effects of the drug (as assessed by observation of the intact animal) were observed.

Life-saving Effect.—If "Nembutal" was administered in a dose exceeding the LD_{50}, no life-saving effect of succinate was observed, whichever way the drug was injected. Intraperitoneal injection under these conditions produced only slight effect; intravenous or intracardial injection early in the narcosis (within twenty minutes of the barbiturate injection) caused a transient period of deeper respiration and stronger heart beat, and occasional twitchings of the legs and ears; but half an hour later the animals were again in deep coma, and the same proportion died as among the controls. Too late injection of succinate, at a time when the respiration had become very irregular and shallow and the heart beat almost inaudible by the stethoscope, produced no effect whatsoever. With doses of "Nembutal" about the LD_{50} or less, the injection of succinate very early after the onset of narcosis caused the temporary restlessness already described without affecting the later course of the narcosis. As a therapeutic procedure too late injection was unnecessary, because the animals had already survived the critical period. However, it appeared that if the succinate was injected just at the moment when respiratory and circulatory collapse was threatening, it helped at least some animals to survive; but this was not statistically significant. It was, furthermore, impossible to ascertain this critical moment exactly. The succinate-treated animals survived a little longer, but the ultimate mortality was scarcely affected.

Analeptic Effect.—When succinate was injected intracardially or intravenously into guinea-pigs under mild barbiturate narcosis (LD_{10} to LD_{20}) lasting three to four hours, it caused distinct "restlessness": increased depth of respiration, often with irregular, deep, gasping inspirations, occasional coughs or groans or clearing of the respiratory tract, with stretching of the neck or contractions of the auxiliary respiratory muscles; increased rate and (stethoscopically audible) strength of the heart beat, often alternating with periods of weaker heart action; twitchings of the hind and fore limbs, and of the ears and nose; opening of the eyes for a few moments, and occasionally a weak lifting of the head. This period of restlessness lasted for about half an hour and ended either in the animal's waking up or in a relapse into deep narcosis, or in a sleep from which the animal could be easily, though only temporarily, roused. After intraperitoneal injection these symptoms were observed to a lesser degree.

Not all animals showed all the symptoms enumerated above, but usually they showed most of them; it must, however, be mentioned that most animals showed one or the other of these symptoms even without having received succinate. The succinate appeared merely to accentuate these reactions and to have a cumulative effect. The symptoms observed may be summarized as non-specific signs of a temporary lightening of narcosis, their actual manifestations varying with the condition and constitution of the animal.

Waking-up Effect.—Guinea-pigs in light narcosis of two to three hours' duration (LD_{10}) were injected about forty minutes after the onset of the narcosis, and the further course of the narcosis was observed. The penetration of the heart wall by the needle caused frequently a jerk of the trunk or of the fore or hind limbs. The first effects of the injection became noticeable towards the end of the injection—often a cough or grunt, followed by a deep inspiration. Some animals opened their eyes, a few raised the head, but none woke up far enough to adopt a sitting position. The animals appeared to be temporarily in a lighter sleep than the controls, but they relapsed into narcosis with the cessation of the disturbance. The final waking-up was not readily ascertained. Most animals were inclined to sleep on. With intraperitoneal injection the effects were still less pronounced.

With rats, however, the result was different. Shortly after the injection they could be roused, like the guinea-pigs, by direct stimulation, but they also dropped quickly back into narcosis. Left alone, they slept for a while, then opened their eyes, began to crawl and sat up, and reacted to stimulation by a sound or a flash of light or from a moving object. They did not again fall asleep. When the time was counted from the moment when the animal dropped into unresponsive narcosis to that when it sat up and took continuous notice of its surroundings, the duration of the narcosis was 20% to 30% shorter with the succinate-treated rats than with the controls. Usually all succinate-treated rats were awake when about half the controls were still lying motionless on their sides. Under the condition of mild narcosis—that is, with a well-functioning circulation—no difference was observed between the effects of intracardial and intraperitoneal injection. However, there were differences between various breeds of rats used. The waking-up effect was more pronounced with a breed of big, spotted, irritable and easily aggressive rats, less with a strain of gentle and rather tame hooded rats of lighter weight.

Degree of Awakeness.—No attempt was made to measure the degree of awakeness by recording devices. The animals were merely observed as to their behaviour and their reaction to stimulation. It appeared that the succinate-treated animals were less drowsy, more accurate in their movements and more aware of their surroundings than the controls, and that they took to food earlier.

Dogs and Cats.

The number of dogs and cats available was not sufficient to allow statistical evaluation of the results. The comparison between the single experiments was rendered difficult by the fact that the animals belonged to different breeds and were very different in temperament. To begin with, the reaction to barbiturate was different. Usually 50 milligrammes of "Nembutal" per kilogram were given first and a further 10 milligrammes per kilogram at ten-minute intervals until narcosis set in. Even so, it was not possible to obtain a reliably comparable depth of narcosis with the different animals. It was therefore not possible to estimate the duration of the narcosis or the rate of survival, and the experiments were conducted mainly with the purpose of establishing whether general or systemic effects of succinate were observed which would add new aspects to the observations recorded with guinea-pigs and rats. The responses observed were variable and inconstant.

Heart and Circulation.—In the decerebrate cat no notable effect was observed on the frequency of the heart beat or on the blood pressure. However, in the intact animals a short arrest of the heart beat followed by irregularity of the beat was frequently noticed. In one dog the heart

stopped during the slow injection of succinate into the femoral vein, and rhythmical compression of the thorax did not resuscitate the animal. In others there was merely a temporary increase in frequency and strength of the beat (Figure I, top left-hand panel). No constant effect could be observed.

Effects on Respiration.—There were usually some effects on the respiration, but they differed in nature as well as in intensity. These effects were as follows: a temporary increase in the depth of respiration, or in the frequency of respiration, or in both (Figure I, top right and left panels); or a more persistent change in periodicity, single deep inspirations alternating with a series of shallow ones; a short arrest in respiration followed by a few very deep inspirations, or a temporary accentuation of existing irregularities (Figure I, top middle panel); or a combination of two or more of these effects. The result of the injection appeared to be identical in the same animal on repeated injections. In one dog respiration stopped abruptly during the third injection of succinate (three millilitres per kilogram) and could not be restored by artificial respiration; the two previous injections of two millilitres per kilogram had caused only a slight increase in the depth and a greater increase in the rate of respiration. In another dog the first injection of three millilitres per kilogram of succinate caused, after a few deep inspirations, a complete standstill of respiration, which quickly responded to a few rhythmical compressions of the thorax. The subsequent regular respiration was about twice as deep as before the injection, and at a higher rate. The effect faded within a few minutes. Two following injections of two millilitres per kilogram each produced a more prolonged increase of the depth and frequency of the respiration (Figure I, bottom panel). In another dog the depth of respiration was initially not affected, but the rate was almost doubled; the depth increased, however, when the rate began to fall.

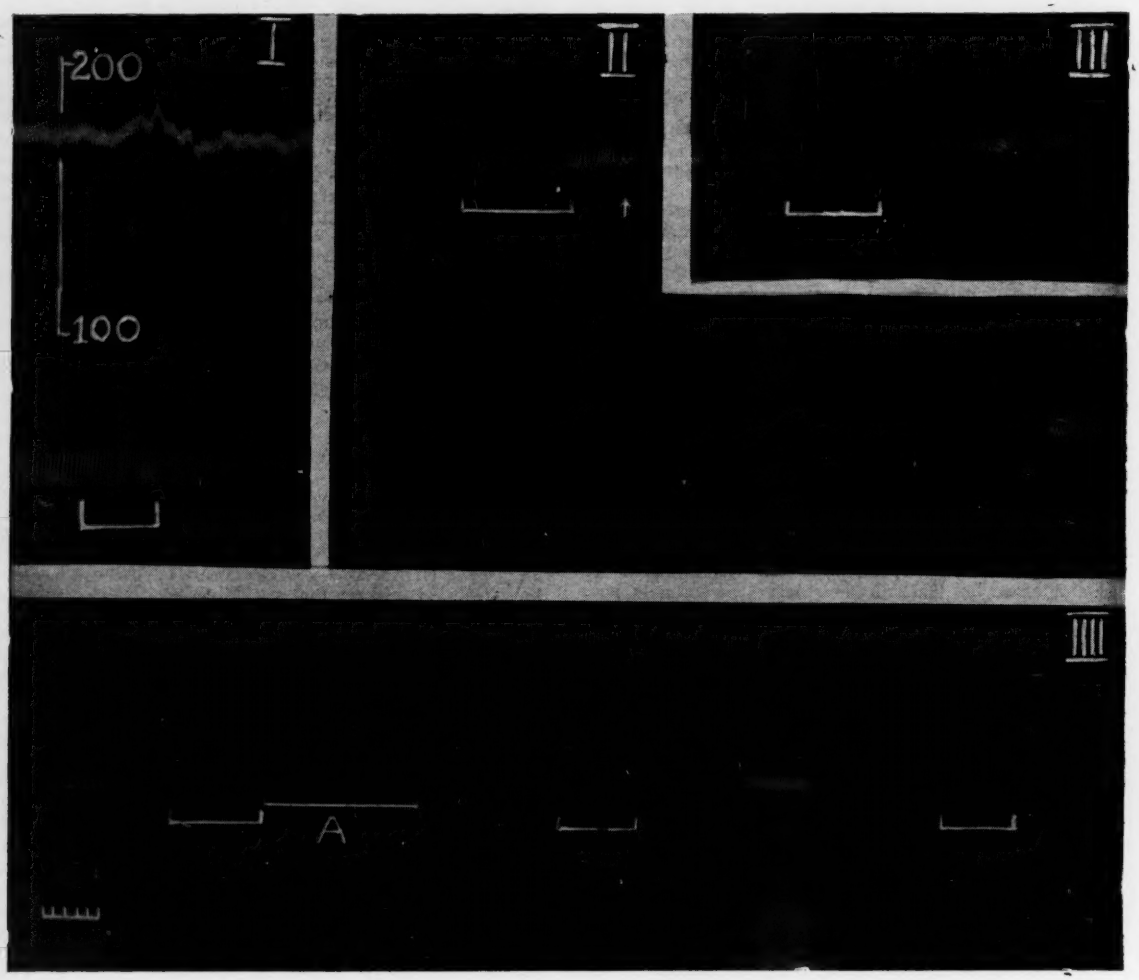


FIGURE I.

I. Top left hand panel, dog. Upper tracing, blood pressure in millimetres of mercury; lower tracing, thoracic movement. At signal third injection of 75 milligrammes of succinate given intravenously. II. Top right hand panel, dog. Thoracic movement; at signal third injection of 75 milligrammes of succinate given intravenously. III. Top middle panel, dog. Thoracic movement; at signal injection of 75 milligrammes of succinate given intravenously. At arrow accentuation of respiratory irregularity resembling an incomplete duplication of the rate, as shown on the lower tracing with a faster revolution of the drum. IV. Lower panel, dog. Thoracic movement; at signals, 75, 78, 75 milligrammes of succinate injected intravenously. At A, artificial respiration. Time marker: 10 seconds.

Reflexes of the Respiratory System.—There was usually, early in the injection, a cough or grunt or clearing of the respiratory tract. The exaggeration of the glottis reflex described by Campbell *et alii* (1948) could not be reliably demonstrated; but the original paper was not available and the procedure may have been different. The tracheal reflex elicited in the decerebrate cat with a feather, which is not affected by barbiturates, ceased in one cat after the injection of succinate.

Effects on the Depth of the Narcosis.—In no case did the animals wake up during or shortly after the injection of succinate, nor did the narcosis itself appear to be less deep and more like a heavy sleep. There were occasional twitchings of the hind limbs and ears; the more frequent movements of the fore limbs were probably due only to auxiliary respiratory muscles coming into action with the distinctly increased depth and frequency of the respiration. However, it is possible that succinate shortens the duration of light narcosis, since some animals were waking up or almost rousable only fifteen to twenty minutes after the injection of succinate, and only twenty-five to thirty minutes after a superficial femoral vein had been exposed without the slightest reaction. After waking up, the animals were possibly less drowsy than would be expected after barbiturate.

After-effects.—All animals which survived the operation were perfectly well on the following day. No after-effects were observed.

Effects on Man.

Here we merely record observations made on man in various clinical conditions after the injection of succinate, and do not at present intend to discuss its clinical usefulness. The dose and concentration employed for intravenous injection was about one-third of that used in animals, usually 50 to 100 millilitres of a 5% (anhydrous) solution. (Higher concentrations are likely to damage the veins.)

Effect on the Healthy and Fully Conscious.

The slow intravenous injection of succinate was found to be free from pain, burning or other sensations. The effects appeared in the following order:

1. Early in the injection, after 10 to 15 millilitres had been given, there was a cough or a short spasm of coughing, rather dry and without expectoration, without any salty or bitter taste, "just a cough". One subject said there was a smell as of a "bad gas", but he was not able to give a clearer description.

2. About the same time an increase in strength and/or frequency of the radial pulse was noticed frequently, though not always. This increase lasted throughout the injection and ceased with it. Deepening of the respiration was often pronounced. This was not due to any mental effort of the subject watching the injection, as was shown in a case of failing respiration (four to five per minute) after lumbar anæsthesia. Fifty millilitres of 5% succinate solution restored the respiration to normal and kept it so for over thirty minutes; then the rate began to fall, but it remained higher than before the injection (by courtesy of Dr. I. R. MacDonald).

3. The most characteristic effect was a bright red flush, which began at the neck and spread slowly over the face and, to a lesser extent, over the arms and the upper part of the trunk, rarely lower. The flush area coincided with the sweat area of the cervical sympathetic. The lower eyelids and the tip of the nose were frequently exempted from the flush and contrasted sharply with the suffused red areas surrounding them. However, there was no constant pupillary reaction or any drooping of the upper eyelid, nor was there a headache or any sign of excitement or other emotional disturbance. The flush was felt merely as a hot, dry, sometimes burning sensation of the skin of the face; in a few cases there was for two to three minutes a feeling of slight dizziness. The onset of the flush was irregular. It occurred never before 15 to 20 millilitres had been injected, but sometimes as late as five to seven minutes after the slow injection of 50 millilitres. The flush reached full development in five to ten minutes and lasted fifteen to twenty minutes altogether. Its intensity varied with the subject, but was about the same on repeated injections in the same subject.

No late effects were observed.

Waking-up Effect.

Deep, Progressing Coma.—Succinate was injected in two cases of prolonged post-operative coma, one following perforation peritonitis, the other cardiac massage after cardiac arrest during the operative treatment of injuries contracted in an accident. Both patients were considered moribund when the injection was given; in neither case was any reaction whatsoever observed.

Waking-up Effect in Hypoglycæmic Coma without Glucose.—Thirty to fifty millilitres of 5% succinate solution were intravenously injected in schizophrenic patients undergoing routine insulin treatment. In all cases the patient showed an early reaction, the single effects appearing, though in varying intensity, in the following order: cough or a spasm of coughing, yawning, opening of the eyes, the deep flush already described starting at the neck and spreading quickly to face, arms and trunk, deeper inspiration and occasionally stronger or faster heart beat, movements of arms and legs, attempts at sitting up, and confused vocalization, followed by a distinct lightening of the coma of three to five minutes' duration. Other irregular effects were the following: a drop of the rectal temperature to a level slightly lower than that of the patients not given succinate (which was in the vicinity of 96° F.), accompanied by shivering, and in one case cardiac arrhythmia, in so far as for several minutes continuously every fourth beat or so was dropped. All patients returned to the previous coma level within ten to fifteen minutes. No later effects were observed.

In Combination with Glucose.—If succinate was injected, either together intravenously with glucose or after glucose given by stomach tube had failed to rouse the patient within twenty to forty minutes, the effects were identical with those described above; but the patients were usually awake, though still confused, towards the end of the slow injection. However, they were distinctly less inclined to violence than those given glucose alone, and they were earlier (within five to ten minutes) well orientated and ready to eat. Their awakening was quicker and less nightmarish, and their temper friendlier. This effect appeared to be constant in the same patient if treatment with and without succinate was alternated.

In Prolonged Insulin Coma.—In a case of protracted coma in which glucose given intravenously failed to rouse the patient, succinate given intravenously (50 millilitres of a 5% solution) awoke the patient sufficiently to talk, drink a cup of tea and eat a sandwich. But half an hour later he relapsed into coma. A second injection after four hours, although the blood glucose level was kept up, showed considerably less effect. A third injection of succinate after eight hours failed to rouse the patient; neither did it produce cough, flush or any other pronounced reaction. The patient awoke after a further twenty-four hours without any noticeable after-effects. In later cases of protracted coma 100 to 150 millilitres of 5% succinate solution were given in the first injection. The patients awoke and stayed awake. None of these cases was grave enough to allow the suggestion of a life-saving effect of succinate.

In Barbiturate Narcosis.—No cases of barbiturate poisoning came under our observation. In cases of schizophrenia in which short barbiturate narcosis (0·5 to 0·7 gramme of thiopental) was preferred to insulin coma, the injection of succinate (20 millilitres of a 5% solution) roused the patient sufficiently to open his eyes, sit up and answer a few questions coherently; after a few minutes he relapsed into a possibly lighter sleep. If the quantity of succinate was increased to 50 or 75 millilitres, the patient woke up with surprisingly little confusion or drowsiness, and remained awake. The effect was identical with that reported by Barrett, and it is not considered necessary to report further observations on this line.

Effect on Confusional State.—In patients who after insulin coma were habitually in a prolonged state of

agitated confusion, disorientation or incoordination lasting up to six or eight hours, succinate, no matter when injected, terminated the condition during the injection or within five to ten minutes. The patients became fully awake and better orientated than they had been before the insulin treatment. The onset of this effect was sometimes dramatically abrupt, in other cases more gradual. The onset did not appear to be correlated with the onset of the flush, nor did the degree of improvement appear to be correlated with the intensity of the flush. This improvement lasted for the day and was often still pronounced in their behaviour on the next morning. On daily repeated injections the effect was maintained, if not increased. Several patients asked for additional succinate treatment because they felt "so rotten" after insulin alone. The effect was constant in the same patient if alternately succinate was given or omitted. The drug acted equally beneficially in confusional states after electro-convulsive treatment and, though to a lesser degree, in confusional or catatonic conditions *per se*. There was, however, little or no immediate improvement of the "schizoid thought pattern". The effect on all these conditions appeared to be fundamentally the same, and consisted in a more objective awareness of and a less distorted response to the surroundings.

"Euphoric" Effect.—Barrett mentions—without, however, stressing the point—that patients awakened by succinate injections from slight barbiturate narcosis (for example, for dental operation) were free from nausea and very soon ready to go home. Vara Lopez (1952) observed the development of euphoria after repeated intravenous injections of succinate. The treatment was tried in several cases of depressive psychosis. One abbreviated case history may be quoted:

Mrs. C.W., aged sixty-three years, has had two previous admissions to hospital, one on April 16, 1936, with a diagnosis of non-systematized confusional insanity. The patient was suspicious and reticent, and her conversation was disconnected. She had 12 "Cardiazol" shock treatments. After her discharge from hospital, she was not able to work and to cope with her family responsibilities. She was readmitted to hospital on May 26, 1939, now depression being the chief manifestation. She stayed several weeks, had 10 "Cardiazol" treatments, and her condition improved; but on her return home symptoms of agitated depression developed again. Her family states that she has been unable to cope with her home duties and her depression has been maintained throughout the years.

On November 5, 1952, she was readmitted to hospital. She was extremely agitated and depressed, weeping easily and unable to concentrate, with pronounced ideas of guilt; she slept poorly and felt hopeless. She had 12 electroconvulsive treatments with no improvement. She was considered for pre-frontal leucotomy.

On December 14 treatment was commenced with succinate given intravenously together with an oral preparation of sodium succinate, one gramme three times a day. After 12 injections of 50 millilitres of a 5% solution, she became less agitated and her symptoms of depression decreased.

On January 30, 1953, after a course of 25 injections, her condition was one in which there was no element of agitation or depression; she occupied herself by playing the piano and was able to conduct a happy, pleasant and witty conversation. Now for the first time she expressed keen interest in going home and rejoining her family. She was discharged from hospital with instructions to continue taking the oral preparation, 1·5 grammes three times a day.

On April 20 the patient and her family stated that she was still well, and her condition on her discharge from hospital has been fully maintained. She is still taking the oral preparation.

Other patients showed the same improvement. However, it would seem that the term euphoria does not adequately describe the change in the clinical condition. The patients, at least with the small doses used, did not show an endogenous, unfounded happy-go-luckiness as seen in some hypomaniacal states; they showed rather a more interested awareness of their surroundings and a readiness actively to participate in them. The general effect was not that depression was displaced by euphoria, but that a more interested attention to the surroundings effaced the tendency to depression.

Oral Ingestion.

The taste of sodium succinate in solution is too unpleasant and nauseating for the medication to be continued over more than a few days. In tablets, however, one-half to two grammes thrice a day after meals can apparently be ingested for weeks without causing nausea, loss of appetite or other gastric trouble. The drug has been used to render the urine alkaline. Koranyi and Szent-Györgyi (1937) held that a daily dose of one gramme of sodium succinate prevented the onset of acidosis, or cured it in diabetics who, despite insulin treatment and controlled diet, inclined to such attacks. In the present work no occasion was encountered to test the claim. On oral ingestion of one to two grammes per day by ourselves, no noticeable effects could be observed. In the investigation presented, intravenous administration was used, since it involved no risk and allowed accurate control of the rate of infusion as well as of the quantity given and of the direct effects. Several patients whose clinical condition had sufficiently improved to warrant their release from hospital have been taking succinate by mouth for four to five months continuously as maintenance treatment. The patients are still well, and it can only be stated that the drug, at a dosage of one to four grammes per day, is certainly not harmful. It is possible that the beneficial effect of a series of succinate injections can at least be prolonged, if not maintained, by oral medication.

Persistence of the Succinate Effect.

The effect of a single succinate injection on confusional or depressed states was found to wear off within a few hours. On prolonged daily medication there seemed to be some sort of cumulative effect which was more persistent. In schizophrenia this improvement could be maintained by daily injections of succinate alone without any additional treatment. However, the improvement was unstable. It persisted through normal sleep or mild barbiturate narcosis; but deep insulin coma brought the patient for several hours or longer back to his original catatonic or confusional state. The underlying condition appeared to be still present and unmodified. It would seem that the patients became more stable as the medication proceeded; but the times of observation are still too short to decide whether the condition became less easily reversible and whether oral succinate medication can displace the injections.

Manometric Experiments.

The oxidation of succinate by various tissues has been widely investigated. No records of such experiments are presented, since they merely repeat and confirm previous work. The experiments recorded here were conducted with guinea-pig brain cells with the purpose of seeing whether, on the addition of small amounts of succinate, the tissue shows, after the period of succinate oxidation, any signs of stimulation or of damage.

If increasing concentrations of succinate, from 0·0025 to 0·02 molar, were applied to guinea-pig brain cells respiring in Krebs phosphate Ringer solution alone, the oxygen uptake was increased *proportionally to the amount of succinate* added. The rate of this increase was highest immediately after addition, but soon it dropped, and the final oxidation rate established after about two hours was in all cases equal to that of the succinate-free control (Figure II). The amount of extra oxygen uptake recorded corresponded satisfactorily to that required for the oxidation of the added succinate to fumarate, and there was no indication that, at these low succinate concentrations, the endogenous metabolism of the tissue was interfered with; it appeared to continue unchanged throughout the one to two hour period of additional succinate oxidation. Only the first impact of the succinate caused a disturbance of the oxygen uptake without apparently interfering with the tissue respiration proper.

If the experiment was conducted in the presence of the glucose concentration commonly used for metabolic experiments (0·01 molar), analogous results were obtained (Figure II, bottom left). The extra oxygen uptake due to succinate was of about the same magnitude as in the

absence of glucose, and the identity of the final oxidation rates was still more obvious, since in the presence of glucose the initial respiration rate is preserved for the time of the manometric experiment.

The presence of barbiturate (0·033 molar final concentration) failed to cause any difference in the amount of extra oxygen uptake due to additional succinate, whether glucose was absent or present (Figure II, right, top and bottom). Neither the respiration of the tissue nor the final respiration rate was affected. There was no indication of any mutual influence or relation between the oxidation of succinate and the metabolism of the tissue.

A series of experiments was designed to see whether different conditions would elicit a stimulating effect of succinate on the metabolism of barbiturate-poisoned brain tissue. Guinea-pigs were injected with "Nembutal", LD_{50}, 60 to 70 milligrammes per kilogram, and killed when coma was well established; the brains were immediately excised and the tissue was transferred into Krebs phosphate Ringer solutions containing a similar or higher concentration of "Nembutal"; succinate was added at the start of the observation in the Warburg flask; or tissue was treated with strong barbiturate for a short time, then washed with Krebs phosphate Ringer solution and equilibrated in the flask, and succinate was added without further addition of barbiturate; or the tissue was first treated with succinate and barbiturate was added afterwards to establish whether its effect was diminished, and any further variations. In none of these experiments were any observations made which suggested a stimulation of the tissue respiration and which would warrant their recording. The succinate was always quickly oxidized, and the metabolic rate of the tissue was always unaffected.

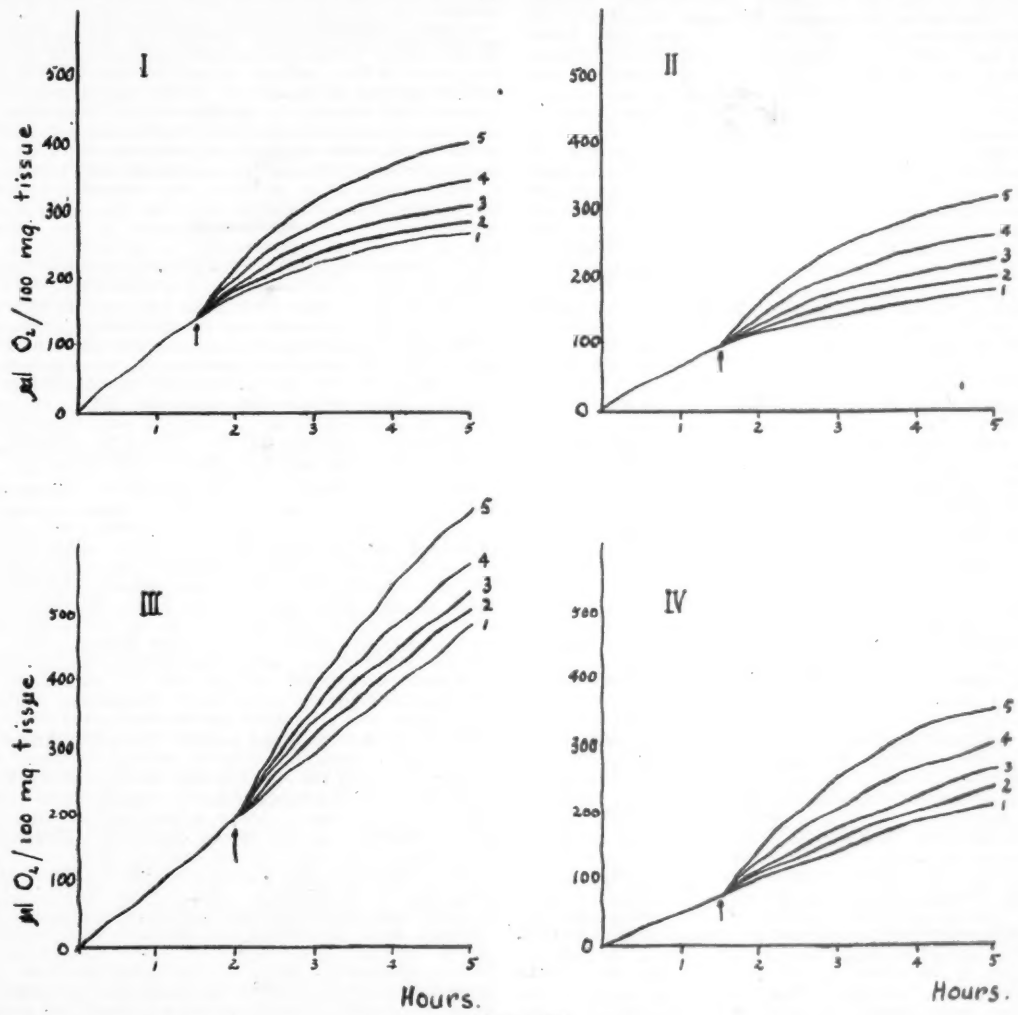


FIGURE II.

Oxygen uptake of guinea-pig brain tissue on addition at arrow of one millilitre of: (i) phosphate Ringer solution; (ii) m/400 sodium succinate solution; (iii) m/200 sodium succinate solution; (iv) m/100 sodium succinate solution; (v) m/50 sodium succinate solution. Warburg flasks; five millilitres total fluid; 37° C.; air; caustic soda paper in centre well; 100 shakings. *Graph I: tissue alone in phosphate Ringer solution. Graph II: same, plus* m/30 "Veronal" solution, final concentration. Graph III: tissue in phosphate Ringer solution containing m/100 glucose solution. Graph IV: *same plus* m/30 "Veronal" solution, final concentration.

DISCUSSION.

The observations presented appear to be contradictory on the following grounds: (i) There was a complete failure to demonstrate in manometric experiments any effect of

added succinate on the endogenous metabolism of surviving cells. (ii) Nevertheless, there were, under some conditions and in certain species, distinct though irregular effects in animals. (iii) Moreover, there were unquestionable effects in barbiturate as well as in other forms of coma and related conditions in man.

The established metabolic function of succinate consists in its role in carbohydrate metabolism, more accurately its role as an intermediate of the tricarboxylic acid cycle. It is outstanding amongst the other intermediates, because its dehydrogenation to fumarate proceeds directly to the cytochrome system, not, like that of the other compounds, over an intermediate, barbiturate-sensitive flavine system (Michaelis and Quastel, 1941). It is therefore not surprising that it is equally readily oxidized in the presence or absence of barbiturate. It is also borate-resistant (Trautner and Messer, unpublished), and owing to the high oxygen affinity and the rapid turnover rate of the enzymes concerned in its oxidation, it is strongly competitive with the other oxidative mechanisms of the cell for the oxygen available. However, Furchgott and Schorr (1948) showed that this rapid oxidation of added succinate does, at least *in vitro*, not contribute to the synthesis of acetylcholine in brain, nor to that of urea in the liver, or deamination in the kidney, or phosphorylation in heart and smooth muscle. Nor does it appear to affect the ammonia and glutamine formation in brain (Trautner and Messer, unpublished). It must be considered whether any effects shown by succinate *in vivo* may be caused through pathways which are not wholly located within the tricarboxylic acid cycle or the maintenance glucose metabolism of the cell. This possibility is strongly suggested by the observation of Mylon and co-workers (1934, 1944) that the injection of succinate or fumarate brings about considerable improvement in the condition of dogs in tourniquet shock, and that this effect is superior to that of glucose; and by our observations that succinate has almost identical effects in hypoglycæmic as in barbiturate coma, and that it roused the patients from prolonged insulin coma or post-comatose confusion when glucose failed to do so.

Before we continue on this line of thought, a notable difference between the conditions *in vitro* and *in vivo* must be discussed. *In vitro*, a small amount of tissue is made to respire in 30 to 50 times excess of fluid containing a concentration of succinate of the order of 0·01 molar, which decreases slowly as the acid is metabolized; *in vivo*, tissue is present in excess over the extracellular fluid and succinate is rapidly injected in a concentration of one to three molar, a few millilitres per kilogram, with the result that the tissue is exposed to the sudden impact of a hypertonic solution of a substance whose rapid oxidation to fumarate will acutely lower the oxygen tension of the blood without a corresponding increase in carbon dioxide evolution (Wolfenberger, 1948). It is plausible that the cough reflex usually observed is a response to chemotactic stimulation and the yawning a manifestation of air hunger; some centre—for example, the respiratory centre—which fails to react to the slow and progressive decrease of oxygen tension which develops in coma, may be stimulated, directly or indirectly, by the sudden anoxia caused by succinate. This assumption of a "respiratory shock" would account for the following observations: (i) most of the immediate effects of the injection were connected with respiration or circulation; (ii) these effects happened only at the very onset of the injection; (iii) there was no effect in the last stages of barbiturate or other coma, in which the respiration was already very shallow and insufficient oxygen was present for rapid succinate oxidation.

However, it will appear that there are other, lasting effects of succinate besides those explained by the shock of the injection. In animals, succinate given by the intraperitoneal route produced almost the same effects as succinate given intravenously; in man, most of the effects were prolonged and different from those of the usual analeptics. The typical flush took three to five minutes before it started to develop, and lasted for fifteen to twenty minutes. The final waking-up was never accompanied by the symptoms to be expected if anybody is, by a violent shock, kicked out of coma into awakeness. On the contrary, the waking-up was gentler, though quicker, than without succinate, and this state of a more pleasant awakeness, awareness and orientation persisted for four to eight hours before the patients relapsed into their usual form of behaviour. Injection in the non-comatose caused, apart from the cough and the hot facial flush, no shock-like, painful, unpleasant or nightmarish sensations, although it lightened the confusional or depressed state if such was present. It must be concluded that, beside its immediate impact, succinate exercises somewhere some lasting specific effects.

Bronk and Brink (1951) observed that low concentrations of chloretone, which lowered the oxygen uptake of resting frog nerve by 15%, reduced by half the increment in oxygen uptake obtained by stimulation at the rate of 50 per second. Johnson and Quastel (1953) showed that narcotics, apart from depressing the respiration, inhibit the oxidative synthesis of adenosine triphosphate, resulting in a reduction of acetyl choline synthesis. It is plausible also that in coma of other origin, or in confusion, the functional metabolism of the cell is more affected than the maintenance metabolism; but it is at the present state of our knowledge difficult to suggest a mechanism by which succinate could affect the functional activities of nerve or other tissue. It could be that, owing to its high redox-potential, the rapidly formed fumarate acts *in loco* as hydrogen acceptor, thus restarting and stimulating or stabilizing a functional metabolism which became stagnant under the conditions of the disease. It could be that succinate (or succinyl-Co A) plays an active role in the functional metabolism of some tissue or tissue system (Sanadi *et alii*, 1953); but there is no actual evidence in favour of these considerations as to the mode of succinate action. There is, however, some evidence as to the possible sites of such action.

The investigations with S^{35} thiopental (Taylor *et alii*, 1949) in the rabbit and the cat did not show any indication of regional accumulation; but this observation does not exclude a regional difference in action. Sahlgren (1934) reported that the effect of injected low concentrations of barbiturates was much stronger in the infundibular region than in any other part of the brain, and Hess (1933) described degenerative changes in the mid-brain on prolonged excessive ingestion (see also Keeser, 1935). This pointer towards one main site of barbiturate action is strengthened by the nature of the succinate effects observed — coughing, yawning, eye-opening, attempted vocalization and stretching, movements of the limbs, flush, awakening, awareness and possibly euphoria. Any of these effects may conceivably be mediated through centres situated between the medulla and the hypothalamus. The assumption that succinate has a specific action on the tissues of this region would help to explain the variety and variability of the effects observed. However, this assumption does not exclude further sites of succinate action. Eichholtz and co-workers (1949) showed that the duration of barbiturate narcosis in adrenalectomized animals was more than 100 times increased and could be brought back to normal by adrenocortical extracts or DOCA. These authors suggest a role of adrenal secretions in overcoming the effect of the drug on those central mechanisms which control consciousness or wakefulness. Such a role of the adrenals could explain the differences which we observed in the succinate effect on the barbiturate coma of man and of animals of different species.

These differences manifested themselves not so much in the coughing, stretching and other responses occurring early in the succinate injection, which seemed to be equally frequent in all animals examined and almost regular in man, as in the awakening response, in which without exception the animals failed increasingly in tameness. Covian (1949) reported that adrenalectomized wild rats required a much higher dosage of DOCA to counteract the effects of stress than the placid laboratory rats. It appears that the wild animal is conditioned to a high activity of its adrenals and depends on it, whereas the tame can do almost, and sometimes entirely, without them. If the overcoming of barbiturate narcosis depends, to some extent, on the response of the adrenals or the adreno-hypothalamic system to the abnormal conditions, and if succinate is able

to "trigger" this response, then the observed differences between experimental animals and man become understandable. The peaceful and habitually sleepy guinea-pigs showed practically no response; with a rather gentle breed of hooded rats some effect of succinate could be demonstrated; and the effect was unquestionable with a breed of *big, easily annoyed and aggressive spotted rats.* Man reacts still more strongly, particularly after the anxiety of an impending operation, and may actually wake up within *ten to fifteen seconds of a slow succinate injection. These* differences in species and within the species may explain why Lardy (1944), Carson (1945) and others failed to notice any effect of succinate on the barbiturate narcosis of their laboratory animals.

It is tentatively concluded that succinate may act on the functional activities of vegetative centres connected with respiratory, cardiac and vasomotor regulation, but also on centres controlling awakeness, awareness and orientation, and the investigation will be continued on lines suggested by this assumption.

SUMMARY.

1. The analeptic effect of succinate has been investigated. Considerable differences were demonstrated in the effects on animals and man.

2. *In vitro*, when guinea-pig brain was used, no stimulating effect of succinate on tissue respiration could be observed under any conditions beside the oxygen uptake due to succinate oxidation itself.

3. *In vivo*, in work on rats and guinea-pigs in "Nembutal" coma (LD_5 to LD_{50}), three millilitres per kilogram of a *30% solution of sodium succinate, hydrated salt, were given* by the intraperitoneal, intravenous or intracardiac route. The responses were: initial cough or grunt and an increase in the strength of the heart beat and depth and frequency of respiration, accompanied by a temporary lightening of the coma. These effects were also shown in cats and dogs, but no dramatic waking effect was ever observed. However, it was found—particularly in rats—that there was a *shortening of the duration of the narcosis by 20% to 25%,* and probably some life-saving effect.

4. In man the analeptic effect in barbiturate coma described by Barrett (1947, 1949) was confirmed by the intravenous administration of 20 to 150 millilitres of 5% solution. *The effects of the injection were as follows: first* a cough or spasm of coughing, then movements of the eyes and the facial and neck muscles, and finally a deep hot flush spreading over the blush areas, lasting up to twenty minutes, the patients waking up during the slow injection.

5. *In hypoglycæmic (insulin) coma of man the patients* showed waking-up effects to the extent of talking and drinking a cup of tea, but relapsed into coma within five to seven minutes. If glucose was given in addition, the waking-up was maintained. Succinate was also effective in *prolonged insulin coma, when glucose alone failed to wake* the patient.

6. In confusional states after insulin coma or electroconvulsive shock the effect of succinate was surprising, as no matter whether the confusion manifested itself in motor restlessness, talking, shouting or weeping, succinate brought the patients within five to ten minutes to a condition of pleasant awareness and more rational orientation. The same effect was observed in confusional, catatonic or depressed states *per se.*

7. The effective doses of succinate caused in the healthy merely a cough and hot flush; but it produced none of the effects of the effective doses of the usual analeptics—namely, excitement, palpitations, convulsions or vomiting.

8. It is tentatively suggested that succinate stimulates the functional activities of some tissue or centres concerned in the regulation of circulation and respiration, as well as of awakeness and awareness.

9. The investigation will be continued with the purpose of further defining the mode of succinate action and its possible usefulness in the clinical conditions mentioned.

ACKNOWLEDGEMENTS.

We wish to thank Professor R. D. Wright, Professor of Physiology, University of Melbourne, and Dr. J. F. J. Cade, *Psychiatrist Superintendent, Mental Hospital, Royal Park,* for their interest in the investigations and for granting facilities for them.

REFERENCES.

BARRETT, R. H. (1947), "The Analeptic Effect of Sodium Succinate on Barbiturate Depression in Man (Conclusion)", *Anesth. & Analg.*, *26*: 105.

BARRETT, R. H. (1949), "Sodium Succinate—An Analeptic for Barbiturate Poisoning in Man", *Ann. Int. Med.*, 31: 739.

BRONK, D. W., and BRINK, F. (1951), "Mechanism Connecting Impulse Conduction and Oxygen Metabolism in Peripheral Nerve", *Fed. Proc.*, 10: 19.

CAMPBELL, C. J., MACS, J. P., and BARRETT, R. H. (1946), *"Sodium Succinate as an Analeptic in Man", from the* Department of Physiological Sciences, Dartmouth Medical School: quoted from *Fed. Proc.*, 5: 15.

CARSON, S. A., KOPPANYI, T., and VIVINO, A. E. (1945), "Studies on Barbiturates XXVIII: Effect of Succinate and Fumarate in Experimental Barbiturate Poisoning", *Anesth. & Analg.*, 24: 177.

*CHAKRAVARTI, M. (1939), "A Quantitative Comparison of Dif-*ferent Analeptics", *J. Pharmacol. & Exper. Therap.*, 67: 153.

COVIAN, M. R. (1949), "Role of Emotional Stress in the Survival of Adrenalectomized Rats given Replacement Therapy", *J. Clin. Endocrinol.*, 9: 678.

EICHHOLTZ, F., HOTOVY, R., COLLISCHONN, P., and KNAUER, H. (1949), *"Beeinflussing der Entgiftungszeiten von Avertin und Pentothal-Natrium an der nebennierenlosen Ratte* durch Nebennieren-Rindenhormon (Pentothal-Natriumtest)", *Arch. exper. Path. u. Pharmakol.*, 207: 576.

FURCHGOTT, R. F., and SCHORR, E. (1948), "Effect of Succinate on Respiration and Certain Metabolic Processes of Mammalian Tissue at Low Oxygen Tensions in Vitro", *J. Biol. Chem.*, 175: 201.

HESS, W. R. (1933), "Der Schlaf", Klin. Wchnschr., 12: 129.

JOHNSON, W. J., and QUASTEL, J. H. (1953), "Narcotics and Biological Acetylations", *Nature*, 171: 602.

KEESER, E. and L. (1935), *"Über die Verteilung der Diäthyl-barbitursaüre im Gehirn", Arch. exper. Path. u. Pharmakol.,* 179: 226.

KORANYI, A., and SZENT-GYÖRGI, A. (1937), *"Über die Bernstein-säurebehandlung diabetischer Azidose", Deutsche med. Wchnschr.*, 63: 1029.

LARDY, H. A., HANSEN, R. G., and PHILIPPS, P. H. (1944), "Ineffectiveness of Sodium Succinate in Control of Duration of Barbiturate Anæsthesia", *Proc. Soc. Exper. Biol. & Med.*, 55: 277.

MICHAELIS, M., and QUASTEL, J. H. (1941), "The Site of Action of Narcotics in Respiratory Processes", *Biochem. J.*, 35: 518.

MYLON, E., WINTERNITZ, M. C., and DE SUTO-NAGY, G. F. (1943), "Studies on Therapy in Traumatic Shock", *Am. J. Physiol.*, 139: 313.

MYLON, E., CASHMAN, C. W., and WINTERNITZ, M. C. (1944), "Studies on Mechanism Involved in Shock and its Therapy", *Am. J. Physiol.*, 142: 299.

SANADI, D. R., and LITTLEFIELD, J. W. (1953), "Studies on α-Ketoglutonic Oxidase: III. Role of Co-enzyme A and Diphosphopyridine Nucleotide", *J. Biol. Chem.*, 201: 103.

SAHLGREN, E. (1934), *"Experimentelle Untersuchungen über den Angriffspunkt des Luminals im Gehirn bei Kaninchen", Acta psychiat. et neurol.*, 9: 129.

SOSKIN, S., and TRAUBENHAUS, M. (1943), "Sodium Succinate as an Antidote for Barbiturate Poisoning and in the Control of the Duration of Barbiturate Anæsthesia", *J. Pharmacol. & Exper. Therap.*, 78: 49.

TAYLOR, J. D., RICHARDS, R. K., and TABERN, D. L. (1949), *"Distribution of Radioactive S^{35} of Thiopental (Pentothal)* in the Rabbit and the Cat", *Anesth. & Analg.*, 29: 105.

VARA LOPEZ, R. (1952), "Succinic Acid in Reiter's Disease", *Brit. Med. J.*, 2: 98.

WOLFENBERGER, A. (1948), "Action of Narcotics and Local Anæsthetics on the Respiration of Heart Muscle", *J. Pharmacol. & Exper. Therap.*, 94: 444.

THE MORTALITY IN AUSTRALIA FROM CANCERS OF THE RESPIRATORY SYSTEM.

By H. O. LANCASTER,

School of Public Health and Tropical Medicine, Sydney.

A BRIEF summary of the mortality from cancer of the respiratory system is given here as part of my survey of *mortality in Australia.*

Definitions.

In this paper, cancer of the respiratory system refers to those cancers arising in the larynx, trachea, bronchi, lung or mediastinum. The years before 1910 are not included in the study, as cancer deaths in this class were distributed

TABLE I.

Trends of the Mortality in Australia from Cancer of the Larynx.

Period.	Sex.	Deaths per Million per Annum at Ages (Years).					
		35 to 44.	45 to 54.	55 to 64.	65 to 74.	75 and Over.	All Ages.
1911 to 1920 ..	M.	5	27	71	119	123	14
1921 to 1930 ..	M.	5	31	90	171	207	20
1931 to 1940 ..	M.	5	27	99	192	271	26
1941 to 1945 ..	M.	3	21	77	177	309	25
1946 to 1948 ..	M.	5	17	66	144	242	23
1911 to 1920 ..	F.	2	7	9	8	12	2
1921 to 1930 ..	F.	1	8	16	19	25	3
1931 to 1940 ..	F.	2	4	18	21	39	4
1941 to 1945 ..	F.	1	4	15	25	34	4
1946 to 1948 ..	F.	0	4	13	26	35	4

over many titles in the detailed tables of *Demography*, the annual publication of the Bureau of Census and Statistics, Canberra. It is convenient to divide all these cancers into two groups—cancers of the larynx and all other respiratory cancers. This second group will be referred to briefly as cancer of the lung, although it contains some cancers of the mediastinum which may have arisen elsewhere. It makes little difference if these cancers of the mediastinum are taken out of the group.

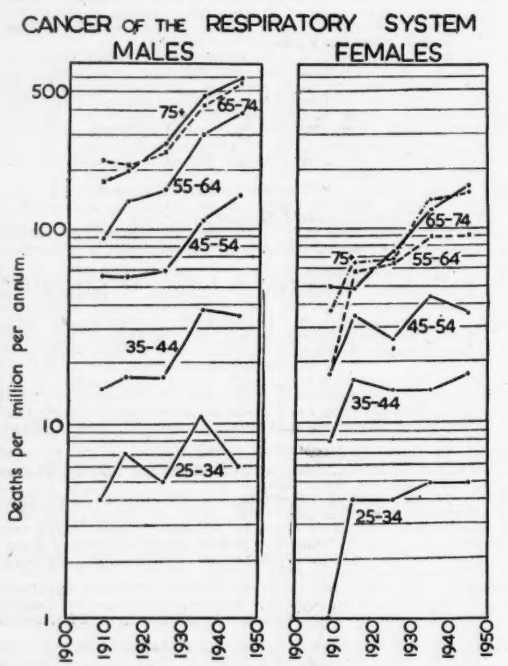


FIGURE I.

The death rates from cancers of the respiratory system in Australia.

Cancer of the Larynx.

In Table I are given the death rates from cancer of the larynx by age and sex. There is the usual increase of the rates with age. There is a pronounced degree of masculinity of the rates, the male rates being over five times as high as the female rates. When the rates at each age are compared for the different periods no definite trend can be noted. There are some slight falls in the rates at ages forty-five to sixty-four years, and some rises at ages over seventy-five years for males, but neither movement is large. The rates for females have remained practically stationary at all ages.

Cancer of the Lung.

Cancer of the lung is taken to include all the cancers arising from any site in the respiratory system except the larynx. This follows clinical phraseology, except in so far as some cancers of the mediastinum so diagnosed may have arisen from sites other than the trachea, bronchi, lung or pleura. The death rates from these cancers are given in Table II. For each period there is an increase in the rates with age and a pronounced degree of masculinity, the male rates being about three times the female rates. At every age there has been a steady increase in the rate since 1920. The rates for the period 1946 to 1948 are almost three times as great as the rates in the period 1911 to 1920. This increase was noted in passing by Doll and Hill (1950), who were studying the causation of a similar increase in England and Wales. Although the Australian rates have risen and cancer of the lung is an important cause of death, in males at any rate, the Australian rates have not yet attained the very high levels now holding in England and Wales. Thus, according to the "Registrar-General's Statistical Review for England and Wales" for the six years from 1940 to 1945, the death rates in 1945 from cancers of the bronchus, lung and pleura were 144 per million at ages thirty-five to forty-four years, 555 per

TABLE II.

Trends of the Mortality in Australia from Cancers of the Respiratory System Other than of the Larynx.

Period.	Sex.	Deaths per Million per Annum at Ages (Years).					
		35 to 44.	45 to 54.	55 to 64.	65 to 74.	75 and Over.	All Ages.
1911 to 1920 ..	M.	12	28	70	92	77	14
1921 to 1930 ..	M.	12	29	69	81	70	16
1931 to 1940 ..	M.	33	85	203	234	208	47
1941 to 1945 ..	M.	32	133	305	388	282	74
1946 to 1948 ..	M.	33	192	452	586	372	112
1911 to 1920 ..	F.	15	27	49	40	53	10
1921 to 1930 ..	F.	18	44	80	95	85	19
1931 to 1940 ..	F.	13	39	74	106	103	21
1941 to 1945 ..	F.	17	32	78	140	127	26
1946 to 1948 ..	F.	18	53	111	148	125	34

million at forty-five to fifty-four years, 1116 per million at fifty-five to sixty-four years, 1050 per million at sixty-five to seventy-four years, and 571 per million at ages over seventy-five years. For females the corresponding rates were 29, 79, 169, 238 and 200. In the present state of knowledge one can only speculate on the differences between the rates in the two countries. Doll and Hill (1952) cite figures giving the annual English consumption of tobacco per head of population as about five pounds. In Australia over many years the consumption has been rather smaller—about three pounds a head. Thus Australian consumption was 3·60 pounds per head in 1908, 3·45 pounds per head in 1928, and 3·37 pounds per head in 1939. Since the war the consumption has risen to 4·70 pounds per head in 1949-1950 and 4·99 pounds per head in 1950-1951.

To find whether there were any geographical variations in the rates in Australia, I have calculated the number of deaths that would be expected in each State if the same death rates held in each State as held in the Commonwealth as a whole. The expected number and observed number of deaths in each of the Australian States approximate closely, so that there does not seem any reason to expect to find a geographical variation in Australia. It seems that research into the incidence of cancer of the lung in Australia might serve as a useful comparison for the English work.

Summary.

There has been little change in the death rates from cancer of the larynx in Australia since 1920. Cancer of the lung has been a more important cause of mortality and is becoming increasingly so. The mortality rates for both forms of cancer have a high masculinity. The mortality from cancer of the lung in Australia is less than that in England and Wales.

Acknowledgements.

This paper is published with the permission of the Director-General of Health, Canberra. Thanks are due to the Commonwealth Statistician for some tabulations of the male cancers.

References.

DOLL, R., and HILL, A. B. (1950), "Smoking and Carcinoma of the Lung; Preliminary Report", *Brit. M. J.*, 2: 739.

DOLL, R., and HILL, A. B. (1952), "Study of the Ætiology of Carcinoma of the Lung", *Brit. M. J.*, 2: 1271.

Reports of Cases.

INFECTION WITH A VARIETY OF SALMONELLA CHOLERÆ-SUIS.

By DAVID G. FAILES and CHARLES E. MARSHALL,
Kanematsu Memorial Institute of Pathology, Sydney Hospital.

SALMONELLA CHOLERÆ-SUIS has frequently been recovered from morbid animals in Australia (Atkinson, 1949), but human infections with this organism are rare, and when they occur tend to be severe. In the case to be described, this organism was isolated from a cerebral abscess both during life and at autopsy.

In infections by *S. choleræ-suis*, septicæmia occurs in about 60% of sporadic cases (Goulder *et alii*, 1942). When localization takes place, the lungs appear to be a site of predilection, for bronchopneumonia develops in about 30% of patients. Purulent meningitis characterized by coma and convulsions has frequently been described.

Ulceration of Peyer's patches in the bowel is very rare. The most usual clinical course is septicæmia with absence of the organism from the fæces. Bronchitis is often noted, and abscesses have been found *post mortem* in various unexpected situations.

Boycott and McNee (1936) describe a case of Salmonella septicæmia, in which the patient died after a febrile illness of two months' duration from purulent meningitis and bronchitis. The organism which they recovered was biochemically identical with that from the case described below.

S. choleræ-suis has occasionally been noted as a secondary invader of tumours (Harvey, 1937).

Clinical Record.

The patient, a woman, aged fifty-two years, was admitted to hospital twenty-two days before death. On her admission to hospital she was aphasic, and no personal history could be obtained; but it was reported that she was a café manageress who had been working continuously for twenty-four hours. She suddenly put her hand to her head and began leaning upon the customers. It was then obvious that she was disorientated and incapable of saying more than "yes" and "no". Apart from a slight head injury eighteen months previously (of which no details could be obtained), the patient had been in good health as far as her relatives were aware.

On physical examination, the patient was conscious, completely non-cooperative and very restless; her pulse rate was 60 per minute; her blood pressure was 200 millimetres of mercury, systolic, and 150 millimetres, diastolic; her respirations numbered 18 per minute, and her temperature was 99·2° F.; albuminuria was present. Apart from slight weakness of the right arm, there were no localizing signs in the central nervous system. There were no abnormal findings in any of the other systems.

A provisional diagnosis of cerebral thrombosis was made, and she was treated with penicillin, 1,000,000 units per day, and general nursing care.

Two days after her admission to hospital the patient had a Jacksonian fit, and several more occurred in the following three days. The right side of the body became paralysed. X-ray examination of the skull revealed displacement of a calcified *falx cerebri*, which indicated a space-occupying lesion of the left side of the cranial cavity.

Her condition improved somewhat four days after her admission to hospital; her temperature, which had been intermittently elevated, now became normal and remained so until operation was performed, and her paralysis disappeared.

Nineteen days after her admission to hospital the patient's condition again deteriorated, and so an arteriographic examination was performed. This revealed a left-sided subdural hæmatoma. Burr holes were made and blood and pus were evacuated, and from this material a species of Salmonella organism was cultured.

After operation there were periods of hyperpyrexia, and the patient died three days later.

During life the hæmoglobin value was 14·3 grammes per 100 millilitres. The leucocytes numbered 7000 per cubic millimetre, 87% being neutrophile cells, 10% lymphocytes and 3% monocytes.

Autopsy Findings.

In the brain there was an infected hæmatoma, with localized abscess formation in the parietal region of the left cerebral hemisphere.

The heart was affected by hypertensive cardio-vascular disease.

In the lungs bilateral suppurative bronchitis was present.

The spleen was enlarged to four times the normal size and weighed 675 grammes. It was very soft in consistency. A culture grew only *Bacillus fæcalis alkaligenes*.

In the gastro-intestinal tract no ulceration was found.

The liver was the site of chronic venous congestion and pronounced fatty change.

In the kidneys the normal pattern was present.

Bacteriological Investigations.

The organism which was isolated during life from the cerebral abscess and again at autopsy from the same site produced the following biochemical and serological results.

Fermentation Reactions.

The fermentation reactions were as follows: acid and gas were produced from glucose, mannite, maltose, sorbitol and xylose; lactose, sucrose, salicin, dulcitol and arabinose were not attacked. Indole was not produced and splitting of urea was absent; hydrogen sulphide was produced after twenty-four hours; motility was present.

Serological Tests.

Positive results to slide agglutination tests were obtained with the organism against the following stock Commonwealth Serum Laboratories antisera: (i) Salmonella "polyvalent" antiserum, diluted one in 50 with saline; (ii) *S. paratyphi* C "O" antiserum, diluted one in 50; (iii) *S. paratyphi* C "H" antiserum, diluted one in 100; (iv) *S. newport* antiserum, diluted one in 50 (presumably a mixture of "O" and "H" antibodies). These results identified the organism as a variety of *S. choleræ-suis*, probably Kunzendorf. It was resistant to penicillin and streptomycin, but sensitive to chloramphenicol, aureomycin and terramycin *in vitro*.

Acknowledgements.

Our thanks are due to Dr. E. H. Stokes, senior physician of Sydney Hospital, for permission to publish the case.

References.

ATKINSON, N., WOODROOFE, G. M., and MACBETH, A. M. (1949), "The Occurrence of Salmonella Types in Australia", *Australian J. Exper. Biol. & Med. Sc.*, 27: 375.

BOYCOTT, J., and MCNEE, J. W. (1936), "Human Infection with the American Hog-Cholera Bacillus: A Third Example in England", *Lancet*, 2: 741.

GOULDER, N. E., KINGSLAND, M. F., and JANEWAY, C. A. (1942), "Salmonella Suipestifer Infection in Boston; Report of 11 Cases with Autopsy Findings in Case of Bacterial Endocarditis due to this Organism, and Study of Agglutination Reactions in this Infection", *New England J. Med.*, 226: 127.

HARVEY, A. M. (1937), "Salmonella Suipestifer Infection in Human Beings; Review of Literature and Report of 21 New Cases", *Arch. Int. Med.*, 59: 118.

AN INTERESTING CASE OF HYDATID DISEASE.

By V. R. HARRISON,
Tumut, New South Wales.

AMONGST interesting cases which one comes across in the course of one's work there is an odd one which would bear reporting. Consequently I put the particulars of the following case forward as being rather unique, owing to the age of the child.

On May 21, 1953, a small child, J.O., aged two and a half years, was brought to me and diagnosed as suffering from acute appendicitis. Later that day an acutely inflamed appendix was removed through the usual incision. However, during the operation an opalescent cyst was seen in the central part of the abdomen lying just below the umbilicus. On gentle traction the whole cyst slipped out into my hand, being only lightly adherent to the anterior abdominal wall and the coils of the small bowel behind. Subsequent pathological examination in Sydney proved this to be a hydatid cyst. Clinically it was an endocyst only, and the light adhesions found at operation may have been the earliest signs of an ectocyst beginning to form.

In view of the age of the patient, only two and a half years, the problem seems to be, how did a cyst the size of a goose egg develop to such a size, and how did it arrive at its final destination free in the abdomen?

TRANSFIXION OF THE EYEBALL WITH RECOVERY.

By T. BOYD LAW,
Lismore, New South Wales.

ANYONE contemplating for a moment the accompanying photograph (Figure I) would in all probability discount any likelihood of recovery of the eyeball either functionally or indeed even anatomically. And yet in the case to be described this actually happened, and after fifteen years the eye still retains its full function as a seeing organ. The eyeball in the photograph has nothing to do with the case but is merely a pathological specimen transfixed by a packing-case needle (identical with the one involved in this case history).

The side of the eye is cut away to show more accurately the approximate track taken by the needle at the moment of transfixion, and how it passed posterior to the lens without even grazing it.

Clinical Record.

Mr. H., aged thirty-two years, while using such a packing-case needle to sew a bag, had the misfortune to jab it into his right eye when the string broke. The needle was withdrawn by himself immediately, and when he was examined by me about two hours later there was a wound a few millimetres long in the horizontal meridian on the medial aspect of the sclera a few millimetres posterior to the limbus. There was also a smaller wound on the lateral aspect of the eyeball similarly situated. Vitreous was protruding from both openings, and this was dealt with and the wounds were closed satisfactorily and, may I say, philosophically.

The development of panophthalmitis was then awaited with confidence. Nothing happened, however, and the eye healed by first intention. It was possible on fundoscopic examination to see the hole in the retina on both sides of the eye with a thin track of pigment particles connecting them across the vitreous.

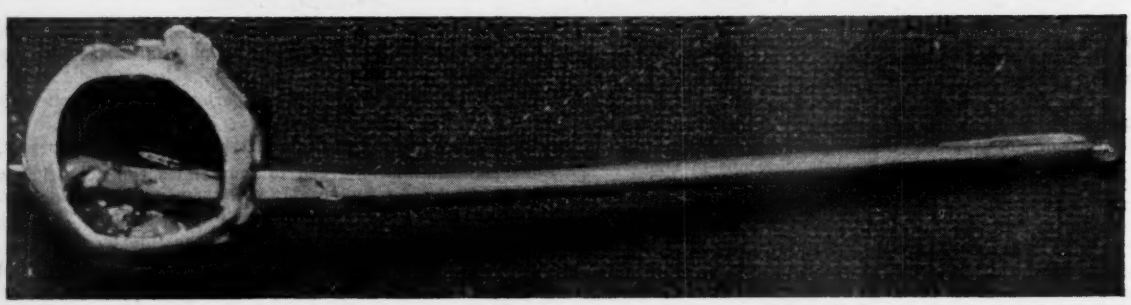


FIGURE I.

The patient remained in hospital with both eyes bandaged for three weeks and was examined from time to time after that. A warning was given regarding the possibility of detachment of the retina and the symptoms to be expected. Again, however, nothing happened.

Mr. H. was examined again in March of this year (that is, fifteen years from the time of the original accident) and the visual acuity of the eye is still 6/6 and he has no disability whatsoever. Externally, it is still possible to see an old scar near the limbus on the medial aspect of the eyeball.

Fundoscopy shows an old retinal lesion on the horizontal meridian in its medial aspect about four millimetres by two millimetres and, on the opposite side of the eye, some slight pigmentary disturbance where the point of the needle has just penetrated the retina.

Comment.

The possibilities of what might have been, ranging from a red eye right through to complete loss, make one wonder at the special dispensation extended to fantastic injuries of this kind.

But then, of course, *"nec scire fas est omnia"*.

Reviews.

Practice of Psychiatry. By William S. Sadler, M.D., F.A.P.A.; 1953. St. Louis: The C. V. Mosby Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 10" x 7", pp. 1184. Price: £7 17s. 6d.

THE "Practice of Psychiatry" is the third of Dr. William S. Sadler's text-books, an impressive volume of over a thousand pages. For a work of this size there is a regrettable lack of factual and statistical information, and much of it gives the impression of a somewhat unsystematic compilation of abstracts from various sources interspersed with personal observations. We found little or no reference to biochemistry or morbid anatomy, presumably deemed out of place in the practice of psychiatry. There is a short account of the subconscious and mental mechanisms, while a more detailed description of personality is placed later in Part V, dealing with personality disorders, and including the psychology and psychiatry of childhood. Special attention is given to the pathoses, described as "a preneurotic group of attitudinal manifestations or mind ego disturbances", to be distinguished from more severe personality disorders. Dr. Sadler does not favour the routine use of relaxants in convulsion therapy. Penicillin is regarded as no more satisfactory than fever therapy in neurosyphilis, but courses of four million units only are recommended. Over a hundred pages are devoted to psychosomatic diseases including disordered sexual functions, but various sex problems are dealt with at greater length in another part of the book. Two hundred and fifty pages comprise Part VII on general therapeutics, in which mental and physical methods of treatment are described in somewhat haphazard fashion. We doubt the wisdom of including a chapter which summarizes the leading schools of philosophy and religious doctrine, unless the reader has already made a study of such matters. Nevertheless the reader will find in this part a wealth of advice as to the handling of domestic, occupational and other stresses. In the preface the author expresses the hope that the work may contribute to making the average physician more psychiatrically minded. We feel that a less ambitious volume would be more successful in achieving that object. If the book is intended for the medical profession, we fail to see why neurosyphilis, *tabes dorsalis*, and Wassermann reaction need to be included in the terminal glossary where also anomia is defined as inability to associate objects or persons with their names. Benjamin Rush coined this word to cover moral defect (a-nomos, lawless).

Medical Electricity for Massage Students. By Hugh Morris, M.D., D.R.M.E.; Fourth Edition; 1953. London: J. and A. Churchill, Limited. 9" x 6", pp. 672, with 113 illustrations. Price: 27s. 6d.

THIS book will be of benefit to massage students and will prove a valuable reference for them after graduation. It is naturally written from the practical angle, and details of all procedures are clearly enumerated, with due emphasis upon the most important phases of electrotherapy. The theories behind the different forms of electrical apparatus are discussed, and where necessary the circuits are illustrated. The chapters on long-wave and short-wave diathermy give an excellent description of the use of this form of therapy and also state the scope and limitations of diathermy, besides giving due warning about the dangers that can arise from the careless use of powerful apparatus. To emphasize further the dangers associated with electro-medical appliances, a list of precautions issued by the Ministry of Health in Great Britain is included. In concluding chapters the diseases which respond to electrotherapy are listed, together with details for the treatment of each malady, and finally a very useful glossary is appended. All physiotherapists will derive much help from this clearly written work, which conveys the lessons learnt by the author after years of practice.

Operative Gynecology. By Richard W. Te Linde: Second Edition; 1953. Philadelphia: J. B. Lippincott Company. Sydney: Angus and Robertson, Limited. 10" x 7", pp. 926, with 409 illustrations and seven plates in colour. Price: £10 15s.

TE LINDE'S second edition of "Operative Gynecology" is noteworthy because of the excellence of the illustrations and the sound gynæcological sense of the text, which condenses the author's wide clinical and operative experience. Te Linde's conception of a gynæcologist as being "a surgeon, expert in his field; trained in the fundamentals of obstetrics; having the technical skill to investigate female urological conditions; having the understanding of endocrinology as it applies to gynæcology; and being well grounded in gynæcological pathology" is amply demonstrated in the trend of this book, which emphasizes that the training of gynæcologists should not swing too far from general abdominal surgery and that gynæcological pathology should be the bedrock on which gynæcological surgery is practised. This book is more than a mere illustrated description of operative procedures, as the advisability of the described technique is explained against a background of experience and pathology.

Prolapse of the uterus is dealt with thoroughly and well and it would appear that the Manchester operation is not recommended when future pregnancies are to be considered, but this would not be a contraindication in this country. However, the author doubts the curative effect of the Manchester operation in *procidentia uteri* and prolapse with a bulky, third-degree retroversion, and his views have some justification. The Watkins transposition and the Spalding-Richardson composite operations are described, but gynæcologists in this country have had little or no experience of them, nor do they seem rational procedures for the problem of prolapse.

It is surprising not to find dyspareunia listed as a possible symptom of retroversion even though it is due to the secondary prolapse of the ovary. One illustration which could be dispensed with is that depicting the time-honoured and oft-condemned ventrofixation.

The author's views on hysterosalpingography strike a very practical note, as the undeniable prevalence of infective complications is stressed, and would seem to reduce the indications for the use of hysterosalpingography in the investigation of sterility.

The chapters on malignant disease are particularly vulnerable to criticism. An excellent discussion of *carcinoma in situ* of the cervix is an addendum in this edition. The operation treatment advised is a modified Wertheim operation, in which the ureters are displayed in their whole pelvic length, the utero-sacral ligaments divided distant from the uterus and the vagina sectioned with an appreciable cuff. The use of ureteric catheters to demonstrate the ureters seems unnecessary and unwise to a practising gynæcologist. This operation is described in detail, yet in the chapter on carcinoma of the body of the uterus the limited total hysterectomy is advocated. Surely this is a retrograde and inconsistent step to depart from the more complete and wider excision, which the modified Wertheim's operation allows, particularly in view of recent thought on body cancer, with its increasing prevalence of endocervical involvement and later developing vaginal metastases.

Te Linde chooses irradiation measures for treatment of *carcinoma cervicis uteri* and he limits the indications for the Wertheim operation with lymphadenectomy to stage one and rarely stage two cases, in which it becomes obvious that the growth is not responding to irradiation. The operative mortality and the risk of ureteric fistulæ would seem to colour his views considerably against surgery. However, in well-established clinics the operative mortality should be negligible and ureteric fistulæ should not occur. The treatment of the ureters in the advocated modified Wertheim operation for cervical *carcinoma in situ* is only slightly different from that in a true Wertheim, as the depth of section of the vagina should not influence appreciably the

degree of dissection and display of the bladder and ureters; yet surgery is proposed for a non-invasive growth and condemned for an invasive growth with probable involvement of radio-resistant lymph nodes.

The book is a handsome volume, full of valuable advice, amply and excellently illustrated and despite the price should have a place on all aspiring and practising gynæcologists' bookshelves.

Australia in the War of 1939-1945: Series Four (Civil); Volume I: The Government and the People, 1939-1941. By Paul Hasluck; 1952. Canberra: Australian War Memorial. Sydney: Angus and Robertson, Limited. 9¼" × 6¼", pp. 662, with 74 illustrations. Price: 25s.

THE official history of Australia in the war of 1939 to 1945 is divided into five series, namely, Army, Navy, Air, Civil and Medical, and consists of twenty-two books in all. The book under review is the first of the five books in the civil series. The second book, dealing with the period from 1942 to 1945, is being written by the same author. Only two other books in the whole of the series had been published at the time of the publication of this volume, while two others were in the press.

Mr. Hasluck's academic qualifications and his experience as a journalist, a university lecturer, a public servant and an officer in the Australian diplomatic service have rendered him most capable of performing satisfactorily the difficult task which was assigned to him. He is, of course, now a member of Parliament and a Commonwealth Minister of State.

In a preface the author points out that the two volumes of the political and social history are part of a series of volumes, and that, although they have been planned to give a self-contained narrative of the main and social events in Australia during the war of 1939-1945, they should be read with the knowledge that other volumes deal with military, naval and air operations, and in particular that the "home front" series of volumes includes two on economic and one on scientific technological developments.

The book now under review covers more than 600 pages and contains thirteen chapters each on a different subject. It is a comprehensive document. The author acknowledges the assistance given him by persons whom he names, who read the whole or part of the manuscript, and by departmental officers and others who facilitated research. Detailed research was concentrated on purely Australian material, and the author limited himself to writing, with conscious narrowness, a history of Australian participation in political events.

Space forbids a detailed examination of the book. The table of contents gives a clear idea of the vast field covered. As is pointed out on the jacket, the volume draws on a wide range of records, and the liberal quotations from documents will make it a valuable source book as well as a valuable narrative. Incidentally, the documents consulted are indicated at the foot of the relative pages and this makes for easy reference. There is a copious index, which makes the book all the more valuable.

The difficulties which confront a government at any time are great, but this book shows how they are increased and intensified during a period of expectation of war and especially when a war is in progress.

Matters of special interest are the controversy between the United Kingdom Government and three successive Australian governments on the subject of the withdrawal of all Australian troops from Tobruk, the attitude of the Labour Party throughout the period covered by the war, the changed attitude of the Communist Party when Russia came into the war, and the great progress made by Australia in the production of munitions *et cetera*.

Mr. Hasluck is fair in drawing conclusions and he is to be congratulated on producing such a valuable historical document and a work which is interesting as well as being informative.

Tumors of Bone: A Roentgenographic Atlas. By Bradley L. Coley, M.D., F.A.C.S., and Norman L. Higinbotham, M.D., C.M., F.A.C.S.; "Annals of Roentgenology"; Volume XXI; 1953. New York: Paul B. Hoeber, Incorporated. 10¼" × 8", pp. 222, with 172 illustrations. Price: $10.00.

THIS book is another of the series of monographic atlases, known as the *Annals of Roentgenology*. It follows the usual course of these atlases, giving a maximum of illustrations with a minimum of text. However, the descriptions given of the radiographs are quite adequate, and the various conditions likely to be mistaken for the lesion illustrated are set out quite clearly. Every tumour likely to be met with is clearly illustrated, and the various infections are also considered. The non-neoplastic conditions, which are so frequently seen, get very close consideration. Practically all the conditions described and illustrated have been confirmed by post-mortem or microscopic examination.

The authors consider that where there is a difference of opinion between the radiologist and pathologist, it is safer to follow the radiologist's opinion. The pathologist is apt to err in the diagnosis of cartilaginous tumours, as the portion examined may not be that section which has malignant changes in it. The illustrations are excellent, with a few exceptions, in which the original negative has been enlarged too much. However, the work is a most interesting and important one and should be of great use to both student and radiologist.

Current Therapy, 1953: Latest Approved Methods of Treatment for the Practising Physician. Edited by Howard F. Conn, M.D.; 1953. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical), Limited. 10¼" × 8", pp. 868. Price: £5 4s. 6d.

THIS book has appeared annually since 1949. The 1953 edition, as before, is edited by Dr. Howard F. Conn. The many contributors are all men of standing and include recognized international authorities. In general it can be said that the expectation of authoritative guidance in a scheme of treatment of almost any medical disorder is realized. Certain blemishes have been pointed out before, and a few can still be found. The dosage of powerful drugs needs more careful checking. That recommended on page 226 for triethylene melamine (TEM) is a dangerous misstatement or misprint; if taken literally it would surely kill the patient. In spite of the contributor's injunction to "adjust the dose with great care to avoid severe marrow depression" he advises a dose of "one-half-gram" and later mentions "0·5 gram amounts". On page 641 it seems that 30 grammes of potassium chloride three times a day are thought to be safe.

Other faults are made up for by the clear and balanced directions mostly to be found. Even surgical, gynæcological, obstetrical and skin conditions are dealt with, although the emphasis is on internal medicine.

The useful roster of drugs remains, and there is a long list of the principal toxic ingredients to be found in various commercial products. Australian readers would like to see the names of some more familiar drugs and drug houses included.

Our good opinion of this book grows with the studying of each successive edition, and (provided he verifies dosages and procedures about which he is uneasy) we recommend it to him who has not so far had it. He can then decide for himself if its rather high price justifies its annual purchase. We are inclined to think that every two years would suffice.

The Science and Practice of Surgery. By W. H. C. Romanis, M.A., M.B., M.Chir. (Cantab.), F.R.C.S. (England), F.R.S. (Edin.), and Philip H. Mitchiner, C.B., C.B.E., T.D., M.D., M.S. (London), F.R.C.S. (England), D.Ch. (Durham), M.Ch. (Cairo); Ninth Edition; 1952. London: J. and A. Churchill, Limited. In two volumes. Volume I: General Surgery. 9¼" × 6¼", pp. 880, with 20 plates and 402 text figures. Price: 32s. Volume II: Regional Surgery. 9¼" × 6¼", pp. 1026, with eight plates and 326 text figures. Price: 36s.

IT is a quarter of a century since this excellent text-book of surgery was first published, and today it has reached its ninth edition. Each new edition has seen the book revised and sections rewritten to keep pace with the increasing scope of the science and art of surgery. As it is four years since the previous edition appeared, these present volumes cover the changes in surgical procedures occasioned by the use of the antibiotics. Also, the chapter on diseases of the eye has been reinserted, and the sections on anæsthesia and surgery of the ear, nose and throat have been largely rewritten. The sections on radiotherapy, venereal disease and plastic surgery have been revised and modified where necessary.

As in previous editions the book is in two volumes. Volume I covers the field of general surgery. Its early chapters are devoted to general principles of surgery and cover those aspects of trauma, infection and neoplasia which can be dealt with in a concise and comprehensive review.

In this section the chapter on ulceration and gangrene is outstanding in its presentation, but that dealing with the surgical aspects of trauma does not attain such a high standard. One feels that surgical and traumatic shock could be approached in a more scientific manner now. Some explanation of the pathological physiology involved would give a better rationale for treatment than "resting the exhausted centres and restoring vitality".

In the portion dealing with burns and scalds one would like to have seen the importance of surface areas stressed (combined with a method for its estimation) rather than the listing of Dupuytren's six degrees of depth. Also, most students and particularly hospital resident medical officers would welcome some guidance and information on the indications for maintenance of intravenous supportive therapy in severe burns.

The chapters which follow deal with surgical lesions involving the skin, the vasculature and aural tissues of the body, all of excellent value. Then follow 10 chapters which give a good survey of bone and joint surgery. After a chapter on plastic surgery come three chapters devoted to some of the companion specialties of surgery. The first of these chapters contains information on X rays in diagnosis. Then an intensively revised and rewritten chapter on radiotherapy offers a helpful presentation of this rapidly advancing field. The last chapter on anæsthesia incorporates the tremendous advances on which the present-day practice of surgery depends so much.

The second volume, covering regional surgery, is comprehensive and of a very high standard. It is sound in general principles, accurate in technical details and stimulating in its clinical descriptions, which are a pleasure to read. The systematic approach used is of immense value to the medical student, and most convenient to those using it as a book of reference.

The pleasant task of reviewing the new edition of this established text-book of surgery is mixed with sadness owing to the death since the edition was published of one of the co-authors, that great teacher of clinical surgery, Mr. Philip Mitchener. Though students will miss his forthright lectures and sound teaching, we are fortunate indeed that his influence will live on in this splendid book.

The Principles of Thoracic Anæsthesia: Past and Present. By William W. Mushin, M.A. (Oxon.), M.B., B.S. (London), M.R.C.S., F.F.A.R.C.S., D.A., and L. Rendell-Baker, M.B., B.S. (London), M.R.C.S., D.A.; 1953. Oxford: Blackwell Scientific Publications. 10″ × 7½″, pp. 190, with 193 illustrations. Price: 42s.

IN its opening chapters, this small volume sets out to describe the mechanical, physiological and anatomical difficulties associated with the administration of inhalation anæsthesia to the "open chest" subject. This is done in a simple straightforward manner. The book goes on to trace historically the development of various means of overcoming these difficulties up to and including the most modern methods.

In this manner, paradoxical respiration, mediastinal "flap", controlled respiration, intubation, broncho-pleural fistula and the management of the "wet lung" case are dealt with categorically.

Emphasis is on the historical aspect throughout, and it is in no sense a how-to-do-it book. Indeed, some of the more difficult technical procedures, such as the management of bronchus blockers and of endobronchial intubation, are dealt with all too briefly. On the other hand, a wealth of detail of the construction of outmoded apparatus is frequently given, almost to the point of being tedious.

The book is profusely illustrated with photographs, diagrams and reproductions of old sketches. The illustrations are beautifully presented and are a feature of the volume.

The book is purely one for the specialist and is worth a place in his library as a work of historical reference. It is not of great practical value to the learner in thoracic anæsthesia, or to the practising anæsthetist as a handbook of reference in his day-to-day difficulties. However, it does what it sets out to do in a clear, forthright manner.

In Appendix II the reader is provided with portraits and short biographical sketches of many names famous in the development of surgery and anæsthesia.

The book is beautifully produced, easy to read and full of interest to the specialist in anæsthesia.

Gifford's Textbook of Ophthalmology. By Francis Heed Adler, M.D.; Fifth Edition; 1953. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical), Limited. 9¾″ × 6¼″, pp. 498, with 26 plates in colour and 281 text figures. Price: £3 11s. 3d.

IN the fifth edition of this text-book the editor, Francis Heed Adler, has taken the unusual step of omitting the chapter on surgical technique; but as the book is intended for the "general physician" the action is to be commended.

There is little to criticize in a volume which attempts in such a commonsense way to demonstrate to the physician the viewpoint of the ophthalmologist. At times the specialist is carried away by enthusiasm for his specialty, as when he urges the clinician to classify his cases of hypertensive disease according to the grading of Keith and Wagner. This may suit the "purpose of uniformity", but it does not conform with the experience of the ophthalmologist who daily observes the normal fundi of hypertensives of all grades.

In spite of an occasional sin of commission, such as the "simple excision" of the head of a pterygium, or of omission, when no reference is made to the dramatic effect of the subconjunctival use of penicillin, this book must be recommended to the general physician as one of the best of its kind. It is surely time that its distinguished editor renamed it "Adler's Text-book of Ophthalmology".

Pulmonary Tuberculosis: A Handbook for Students and Practitioners. By R. Y. Keers, M.D., F.R.C.P. Edinburgh), F.R.F.P.S. (Glasgow), F.R.S.E., and B. G. Rigden, M.R.C.S. (England), L.R.C.P. (London), with a foreword by F. H. Young, O.B.E., M.D. (Cambridge), F.R.C.P. (London), D.P.H.; Third Edition; 1953. Edinburgh: E. S. Livingstone, Limited. 7½″ × 5″, pp. 340, with 150 illustrations. Price: 24s.

THIS third edition, written six years after the second, maintains the high standard of its predecessors. In a previous review, criticism was made that in such a chronic disease as tuberculosis major developments were unlikely to occur over short periods of time. In the past six years, however, major developments in almost all aspects of tuberculosis have taken place every few months or so, and much of the old edition has therefore been rewritten. In effect, the chapters concerned with bacteriological examination, examination of the patient, treatment including collapse therapy, surgery and chemotherapy, complications, rehabilitation and prevention have all been revised or rewritten. However, changes have occurred so rapidly that, as the authors themselves remark, by the time the book was published, much that was written was out of date.

It is, of course, easy to be critical of many statements written in any text-book. It is surprising, however, to read the statement that "so far as adults are concerned, the routine use of tuberculin testing as a diagnostic measure, has ceased". It is realized that the infection rate in the cities of England, Scotland and the Continent is quite high for adults, but this does not hold for countries such as parts of America and Australia. As a pointer to the incidence of infection, the tuberculin test is most valuable indeed, and its value will increase as the disease is controlled. Furthermore, a negative Mantoux test result in this country has saved many an adult patient from a possible mistaken radiological diagnosis of tuberculosis.

Despite these comments, the handbook is truly excellent for the student and the practitioner to brush up his knowledge. It could well be in the hands of every doctor.

Textbook of Virology: For Students and Practitioners of Medicine. By A. J. Rhodes, M.D., F.R.C.P. (Edinburgh), and C. E. van Rooyen, M.D., D.Sc. (Edinburgh), M.R.C.P. (London); Second Edition; 1953. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 9″ × 6¼″, pp. 576, with 76 illustrations. Price: £4 6s.

THE first edition of this book, which appeared in 1949, was recognized as a standard manual on virus diseases of man. During the last three years, there have been considerable advances in virology, so that this second edition contains much new material. In addition several sections have been extensively revised.

The book will be particularly attractive to general practitioners, as well as to undergraduate and post-graduate students of virology. The addition of a selected bibliography at the end of each chapter will be of great assistance to those desiring more extensive reading.

The first section of 120 pages is devoted to a discussion of the fundamental characteristics of virus infections and the techniques appropriate to their investigation. The remainder of the volume considers the known virus and rickettsial diseases of man, each disease being grouped according to the predominant clinical manifestations. With one or two minor exceptions, the text is restricted to those virus diseases which affect man, either commonly or rarely. The clinical descriptions are amplified in many cases by illustrations of typical patients; these descriptions, together with a brief consideration of the epidemiology of each disease, will be appreciated by medical practitioners interested in public health work. Details are given of materials available and procedures applicable in immunization against the commoner diseases. Laboratory procedures for the diagnosis of each virus disease are described in general terms. This should allow practitioners and students to obtain a sound conception

of the laboratory work entailed. There are more detailed instructions regarding the collection, preservation and dispatch of material to a virus diagnostic laboratory. Short descriptions are given of the physiology and other characteristics of the commoner viruses, and of the immunity reactions usually evoked by the viruses. Excellent electron micrographs are produced, particularly in the sections dealing with the pox viruses.

The volume is written from the University of Toronto; the perspective of the book is that developed in the virus laboratories of North America. This is particularly apparent in the sections dealing with the specific treatment of viral and rickettsial diseases. In those fields with which we are most familiar, recent advances in virology (Canadian, American, European and Australian) are adequately discussed, and the facts and opinions quoted are those most recently available.

Handbook of Orthopædic Surgery. By Alfred Rives Shands, junior, B.A., M.D., in collaboration with Richard Beverly Raney, B.A., M.D.; Fourth Edition; 1952. St. Louis: The C. V. Mosby Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 9" x 6", pp. 644, with 192 illustrations. Price: £4 4s.

THIS small book of some 500 pages contains a great deal of sound information on orthopædic surgery. The author calls it a handbook, the purpose of which is "to present to the medical student and general practitioner the fundamental facts of orthopædic surgery as concisely as possible and yet in sufficient detail to convey a well-rounded knowledge of the subject". This object is admirably fulfilled.

There are few subjects not mentioned in the text, although the less common conditions are discussed but briefly. The text is followed by 76 pages of bibliography referring the reader to articles in which more detailed information can be found. It is probably natural that the bulk of these references should be to articles by American authors, but one rather regrets the infrequency with which British authors and their works are quoted. Nevertheless, it provides a very useful index and fills in gaps necessarily left in the text—gaps inescapable in a handbook if it is to fulfil its stated role.

The illustrations are mostly line drawings and reproductions of X-ray films. Most of the drawings serve their purpose quite well, but those on pages 273 and 318 might well be replaced.

In spite of these few criticisms, there is much to praise in this little book, which can be thoroughly recommended to all who need to know the main principles of orthopædic surgery without becoming immersed in a mass of detail. Here they will find a plain story concisely told.

Notes on Books, Current Journals and New Appliances.

Family Doctor. Published monthly by the proprietors, the British Medical Association, Tavistock Square, London, E.C.1. Sole agents for Australia and New Zealand: Gordon and Gotch (Australia), Limited. Subscription for twelve months: 20s. (sterling), including postage.

THE November "Family Doctor" greets us delightfully with, on the front cover, a tousled-haired, freckle-faced miss who epitomizes positive health. The editor uses her as a pictorial text for a cheerful discussion on freckles which should start everybody off in a good mood. This is followed, under the heading "Family Reading", by a simple, sensible article on the psychological aspects of dreams, a potpourri of interesting notes under the title "Close-up of Science", a short account of a successful venture in providing for the needs of old people in England, and a brief discussion on the sight of children. The section on "Medicine and Health" has articles on pneumonokoniosis and silicosis, chiropody as a career, alcoholism, and the dogs who are trained to guide the blind. Finally, in the section on the home and family, there is a reference chart for mothers dealing with details of infectious diseases, a selection of attractive photographs of readers' children, articles on draughts in the house and feeding the family in wintertime, cooking hints on soups, stews and casseroles, and further articles on the problems of retired people and the approach to breast feeding. Book reviews, expert advice in answer to readers' questions, and letters from readers make up a full measure. The standard of this excellent popular monthly is well maintained. We would remind our readers that a free sample copy will be sent to any doctor who would like to see one, on application to the Editor of THE MEDICAL JOURNAL OF AUSTRALIA.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Atomic Medicine", edited by Charles F. Behrens, M.D.; Second Edition; 1953. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 9" x 6¼", pp. 646, with 130 illustrations. Price: £5 18s. 3d.

Contains 22 chapters dealing with every aspect of the subject, attempting "to set forth, most undramatically, the authoritative information the physician and all those concerned with civilian defense should have at their disposal at this time".

"Roentgen Diagnosis of the Heart and Great Vessels", by Erich Zdansky, M.D., translated by Linn J. Boyd, M.D., F.A.C.P.; 1953. New York: Grune and Stratton. 10" x 7", pp. 510, with 334 illustrations. Price: $15.50.

This is the first American edition; four years have elapsed since the appearance of the last German edition.

"Pediatrics", by L. Emmett Holt, junior, and Rustin McIntosh; Twelfth Edition; 1953. New York: Appleton-Century-Crofts, Incorporated. 10" x 7", pp. 1502, with 271 illustrations. Price: $15.00.

There are 72 contributors to this work, the first edition of which was published in 1897.

"Stedman's Medical Dictionary: Of Words Used in Medicine with their Derivations and Pronunciation Including Dental, Veterinary, Chemical, Botanical, Electrical, Life Insurance and other Special Terms; Anatomical Tables of Titles in General Use, the Terms Sanctioned by the Basle Anatomical Convention; the New British Anatomical Nomenclature; Pharmaceutical Preparations Official in the U.S. and British Pharmacopœias or Contained in the National Formulary; Biographical Sketches of the Principal Figures in the History of Medicine", edited by Norman Burke Taylor, V.D., M.D., F.R.S.C., F.R.C.S. (Edin.), F.R.C.P. (Can.), M.R.C.S. (London), in collaboration with Allen Ellsworth Taylor, D.S.O., M.A.; Eighteenth Revised Edition; 1953. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 10" x 7", pp. 1606, with 22 plates, three in colour, and many text figures. Price: £6 3s. 6d.

The nature of the work is implicit in the full title.

"Stress Incontinence in the Female", by John C. Ullery, M.D., F.A.C.S., F.I.C.S.; 1953. New York: Grune and Stratton, Incorporated. 10" x 7", pp. 168, with 82 illustrations. Price: $6.75.

Intended primarily for the "medical student or general practitioner who wishes only a general acquaintance with the subject".

"Basic Pathology and Morbid Histology", by D. B. Carter, M.A., M.D. (Cantab.), F.R.C.S. (Eng.); 1953. Bristol: John Wright and Sons, Limited. London: Simpkin Marshall, Limited. 9½" x 6½", pp. 338, with 266 illustrations. Price: 42s.

The book is designed to help the student who has just begun the study of pathology.

"Textbook of Physiology and Biochemistry", by George H. Bell, B.Sc., M.D. (Glasg.), F.R.F.P.S.G., F.R.S.E., J. Norman Davidson, M.D., D.Sc. (Edin.), F.R.F.P.S.G., F.R.I.C., F.R.S.E., and Harold Scarborough, M.B., Ph.D. (Edin.), F.R.C.P.E., with a foreword by Robert C. Garry, M.B., D.Sc. (Glasg.), F.R.F.P.S.G., F.R.S.E.; Second Edition; 1953. Edinburgh and London: E. and S. Livingstone, Limited. 10½" x 6½", pp. 1014, with many illustrations. Price: 50s.

The first edition appeared in 1950.

"Surgery of Repair as Applied to Hand Injuries", by B. K. Rank, M.S. (Melbourne), F.R.C.S. (England), F.R.A.C.S., and A. R. Wakefield, M.S. (Melbourne), F.R.C.S. (England), F.R.A.C.S., with a foreword by Gordon Gordon-Taylor, K.B.E., C.B., LL.D., Sc.D., F.R.C.S., F.R.C.S. (Ed.), F.R.A.C.S., F.A.C.S., F.R.C.S. (Canada); 1953. Edinburgh and London: E. and S. Livingstone, Limited. 10" x 7", pp. 240, with 188 illustrations, one in colour. Price: 40s.

The work is "meant primarily for the discriminative interest of those who see and treat hand injuries".

"Konversion und Reversion klinischer Neurosen: Ein Beitrag zur Pathologie der Furcht Versuch einer Neurosenkunde aus der Praxis des Internisten", by Hans Rehder, M.D.; 1953. Köln: Ärzte (Publishers). 8¼" x 6", pp. 232. Price: 12.90 marks.

Intended for clinicians who have to investigate early forms of neurosis.

The Medical Journal of Australia

SATURDAY, DECEMBER 5, 1953.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: surname of author, initials of author, year, full title of article, name of journal without abbreviation, volume, number of first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

GENIUS.

In March of this year attention was drawn in these columns to a remarkable book by David Wechsler entitled "The Range of Human Capacities". Wechsler asked whether the difference between an Einstein, a Pasteur and a Shakespeare on the one hand and an average man on the other was real or only apparent; and by how much could and did individuals differ from one another—in short, he asked whether there was a limit to human variability, and if there was, whether the limit differed from one trait and ability to another, or whether it was equal in all directions. Wechsler reported an enormous number of observations and measurements and submitted them to careful scrutiny. With regard to the significance of his findings, he stated three possible inferences: (i) The range of human capacities, when calculated in true units of amount, is exceedingly small. (ii) There are calculable limits to human variability, which very probably are biologically determined. (iii) These limits partake of the characteristics of natural constants. At the end of our discussion on Wechsler's book we referred to several other aspects with which he had dealt. Among these was the question of genius and deficiency. Further reference to this question at a later date was indicated.

The title of Wechsler's chapter, "Genius and Deficiency", he thinks is slightly misleading. His intention is not to inquire whether genius is or is not, as some have held, a special pathological condition allied to one or another form of morbidity, but to extend his investigation about the way in which the very superior and the very handicapped differ from those who are neither the one nor the other. We do not propose to follow him too closely in his argument. Rather would we deal with the fascinating subject of genius. We must admit that it is a fascinating subject; in other words, we want to know what it is which gives to a genius his clearness of vision, his unerring discrimination and his creative powers. Many definitions of genius have been given. We are no doubt all familiar with the statement that genius is characterized by an infinite capacity for taking pains. We are no doubt also all agreed that this statement is much wide of the mark. In 1927 a book on genius by Arthur C. Jacobson was reviewed in this journal, and on that occasion we quoted the definition by the late F. Guy Griffiths that genius was a capacity for doing with ease what others did with pains, and for doing with pains what others could not do at all. The "Encyclopædia Britannica" states that genius has become the regular English word for "the highest conceivable form of original ability, something altogether extraordinary and beyond even supreme educational prowess, and differing in kind apparently from 'talent', which is usually distinguished as marked intellectual capacity, short only of the inexplicable endowment to which the term genius is confined". Wechsler states that it is easier to furnish undisputed examples of genius than to give an inclusive definition, and he refers, as one would expect, to Da Vinci, Shakespeare, Pasteur and Edison. He points out that genius is what the German philosophers call a *Grenzphänomen*, a limiting phenomenon. He adds that in the definition of such ultimates we can only emulate the wisdom of Saint Augustine when asked to define time, and answer with him: "I know it when you ask me not." Jacobson put forward the view that a genius might reside in the secondary personality of a person of superior mental endowment—that is, in the unconscious mind. He writes: "The genius is a superman whose creative spirit resides, not in the primary self but in this secondary personality." He thinks that there is nothing in the primary self of the genius to account for his creative powers save his superior mind, which is a *sine qua non* for the successful operation of a genius-endowed secondary personality. "Once the shifting of the gears has been effected, this type of mind affords a delicately attuned *instrument* for the facile operation of the latent power residing in the secondary personality. Successfully set free—*sublimated*, as the Freudians say—this becomes creative power, or genius manifest in works." He sees a striking analogy between a Wagner or a Shelley in the throes of creative activity, oblivious to all about him, the primary self completely eclipsed for the moment, fairly possessed by his *dæmon* or secondary self on the one hand, and the medium in a trance on the other. He states that Mozart declared that his music came to him without his volition, as if he had composed it in a trance. Wechsler believes that the *sui generis* theories of genius have arisen because those who hold them fail to perceive that qualitative changes may result from purely quantitative variations or difference in rate of change in the same process or phenomenon. He thinks that beyond certain points even slight differences in efficiency of an individual's ability may so alter the character of the resulting performance as to make it appear an achievement of an entirely different order or even kind. He is compelled to reject all explanations of genius which call for the intercession of a mystical something, a superhuman touch or *sui generis* traits—all "divine spark" theories. He thinks that we are compelled to look for the explanation of genius in terms of some sort of superiority or unusualness in degree of ability. With regard to superiority, he refers to what he calls the theory of critical differences.

According to this, genius, whilst still a summary term for unusual superiority, also implies a qualitative distinction—a distinction which arises not because we are dealing with a new species of ability, but from the fact that when human capacities surpass certain levels of performance, the achievements to which they give rise may take on altered characteristics. He thinks that the concept of superiority which enters into the definition of genius has a threefold connotation. First, there is a general "comparative connotation of *very-much-more-than* to a superlative degree"—the superior person can do very much more of, or very much more quickly or very much better the kind of thing which the average person can do only in a moderate degree. Secondly, the superior person is a rare person, and finally, superiority of an individual to warrant the classification of genius must be in a field or type of performance which is humanly esteemed in and for itself. It will be clear that the ideas put forward by Wechsler, though they may appear to be, are not incompatible with those of Jacobson. If we accept Jacobson's ideas, it will be necessary in some instances to postulate the existence of some trigger mechanism which will release the unconscious mind and allow it to function. He refers to alcohol as one substance which does the necessary action. It is known that certain literary geniuses have used alcohol deliberately to produce literary fruit, and the *spes phthisica* is known in certain individuals to be the unlocking mechanism. This does not mean that an unlocking mechanism is always necessary. One can imagine that in some persons the fire of genius burns so brightly that no mechanism comes, or has to be called, into action to reveal it. It has been said that what one man does with ease another may do with difficulty—this is talent; but that when a man does what a talented person cannot do—that is genius. Genius is creative. Talent gives out what it has received, what it has collected and understood. The offerings of genius arise from the creative mind; they are poured out because they must be. The fruits of genius cannot be dammed back—the creator must create. There is an exception when some "trigger mechanism" has to come into play. In Jacobson's view the trigger mechanism may be always present in some persons, though he does not actually make the statement—for example, in those geniuses who have been subjects of a tuberculous infection; he gives many names of tuberculous geniuses.

Men of genius judged by every-day standards often appear to be queer people; they may say and do extraordinary things and sometimes can "get away with" what would be more than frowned upon if their doings were those of ordinary folk. This points to the reason why genius and degeneracy or insanity are often linked together in discussion. This aspect of the subject must be raised. Both Wechsler and Jacobson reject the idea that there is any identity between genius and degeneration; unfortunately we cannot follow their arguments in detail. Wechsler bases his view on the fact that quantitative variations may give rise to qualitative differences—the actual mechanism of transformation is at present "hard to conjecture". Jacobson states that the view that the true genius is necessarily crazy is essentially vulgar. He thinks that there is a failure to distinguish between the insane temperament and actual insanity—this is "too fine a distinction for the bourgeoisie of science"—but that it is nevertheless a vital point. Still finer is the fact that the insane temperament itself, only less than actual insanity, is a handicap to the genius and not his "motive force". The genius is usually, he states, if not always, of insane temperament, but his creative work reflects the man at his best, that is to say, at his sanest. Insanity is the Nemesis of the delicately balanced genius, and he does his work not because of, but in spite of, the Damoclean sword. He quotes Weininger: "The genius which runs to madness is no longer genius." The following paragraph by Jacobson may be quoted with advantage:

> Degenerate stock manifests an affinity for the genius which normal breeds lack. This is only a putting of peculiar soil to glorious use. This soil cannot be identified with the flower that it bears. It is thrillingly perilous horticulture; the most precious thing in the world has to be entrusted to gardeners whose aspect is of a most sinister character, but who seem to be the luckiest of husbandmen. Commonplace stock, on the other hand, can never be put to any but commonplace uses. Genius is a supernormal endowment resident in a tenement of dubious but affinitive antecedents.

What then are we to do about the geniuses of the world, these people who are seldom if ever found among the respectable "humbugs and exhibitionists of good family"? Nowadays there is a tendency to a levelling down in education and most other human activities. Humanity owes most of its culture and its so-called progress to its geniuses, and if we try to turn everyone out in the same mould the eruption of genius may became rarer. It is true that gifted children are given special opportunities to equip themselves for life, but they are probably to be included among the talented men and women of the future rather than among the geniuses. Society must see to it that control does not become so heavy that the man or woman with the spark of genius is prevented from following his or her bent. It is a devastating thought that the direction of eugenics and hygiene is towards the elimination of genius; but genius will never be suppressed and, of course, eugenics and hygiene will never reach their perfect fulfilment. We shall therefore not be running with the hare and hunting with the hounds if we wish to see genius given its head and at the same time respect the teaching of eugenics and strive for the perfection of hygiene.

Current Comment.

THE EVOLUTION OF CHILD CARE.

TODAY there are chairs of child health in the great majority of the medical schools of the United Kingdom. The first pædiatric chair was established in 1906, when Sir Frederick Still was appointed professor of diseases of children at King's College, London. The first medical school to emphasize health rather than disease was Edinburgh, which established a chair of child life and health in 1930. Most of the remaining chairs have come into being since the second World War, as has the chair of child health in Sydney, the only one in Australia. This recent rapid acceleration of interest in child health and welfare serves to emphasize the tragic indifference to the subject in past centuries. That this has been a particularly dark page in the history of man's inhumanity to man was well brought out by Professor J. L. Henderson[1] in his

[1] *Lancet*, August 8, 1953.

inaugural address in the new chair of child health in the University of Saint Andrews, delivered in February of this year. He points out that the story of the evolution of child care is the story of the evolution of civilization itself. In primitive society, the welfare of children receives scant attention because the struggle for existence is paramount, and the weakest inevitably go to the wall. The children of ancient times fared best when they were born into a matriarchal society, such as those of Egypt and Babylon, India and China. They were less secure in the later patriarchal civilizations of Greece and Rome and, indeed, also in China and India when the earlier matriarchy went out of fashion. Economic factors have always played a fundamental role in the attitude of society to child life, as Professor Henderson states, though the force of the impact of unfavourable economic circumstances on the child varies with the degree of civilization; "the child is the first to suffer in primitive society, but the last to do so in modern Christian communities". Professor Henderson traces the attitude towards child care through the successive civilizations, and then, century by century from the Renaissance, in Europe and Britain. The detailed story need not detain us now, but it is well to remember that an enlightened attitude towards children in general in our Western civilization has been developed only during the past century, beginning with the notable work of people like Shaftesbury and Barnardo. Other important contributions to progress in this direction, less familiar to us, were also made on the Continent, as Henderson well brings out. The harvest is to be seen in the increasingly favourable state of child health during the last half-century, partly reinforced in the last two decades by the rapid advances in medical science. Most notable has been the dramatic fall of the infant mortality rate in all progressive countries. Henderson states that it is unlikely that further improvements in the standards of child care in the second half of this century will be as great as those which have been achieved in the first half, but this belief is no cause for complacency, for there are still many aspects of child care which call for improvement. Unsatisfactory aspects listed by Henderson include the effect of inferior social conditions, particularly bad housing amongst people of the lower social grades, the continuing high loss of infant life at the time of birth, the employment of mothers of young families in industry, and the loosening of family ties and increasing moral laxity in modern life. The black record of the past centuries and the remarkable progress of the past decades should, each in its own way, serve as a stimulus to the remedying of these remaining defects in our attitude towards child care.

PSYCHIATRIC ASPECTS OF ASTHMA.

To comment upon a paper which purports to do no more than review the literature is to risk doing an injustice to all sides. However, when the paper in question is a critical review by a psychiatrist of psychiatric literature upon so common a problem as asthma, and when this appears in a journal which is not readily accessible,[1] the attempt seems justified. Denis Leigh bases his conclusions, some of which will be summarized, on a review of the literature over the past eighteen years, and on his own four years of experience with eighty adult asthmatic patients at the Maudsley Hospital. He considers that despite a number of contributions on the subject there is little evidence for the existence of an "asthmatic personality", even when allowance is made for the difficulties in assessing personality objectively. Some writers have claimed that there is some reciprocal relationship between psychosis and asthma, with the frightening corollary that psychotherapeutic measures in the asthmatic stage might precipitate psychotic manifestations. This is not confirmed by other authors, and Leigh concludes that the association between psychosis and asthma is probably no greater than might occur by chance. There is no recent satisfactory study of the occurrence of psychiatric symptoms in asthmatic patients, which is unfortunate in that these are the symptoms which usually lead the general physician to refer asthmatics to psychiatrists. On the other hand, there seems to be a high incidence of psychoneurosis or other mental abnormalities in the families of asthmatic patients. Emotional stimuli undoubtedly frequently precipitate—and occasionally abort—asthmatic attacks. These stimuli may be grouped: (*a*) sudden intense emotion (anger, fear), (*b*) sexual conflicts, (*c*) disturbance of dependent relationship (the commonest of which is certainly that between mother and child), (*d*) danger to a relative, (*e*) fear of respiratory disease or identification with the dyspnœic attacks of others, (*f*) real or imaginary "gain" in the psychological sense. None of these is necessarily specific for any one patient, and, in fact, emotional stimuli, in Leigh's view, are only one of a group of factors —endocrine, allergic, metabolic—which may upset an equilibrium and result in the precipitation of an attack.

Leigh mentions a point which is frequently given insufficient emphasis: sudden death in *status asthmaticus* is by no means rare, and in his view no patient in *status asthmaticus* "should be denied a psychiatrist". Although he could find no other cases in the literature, he records the death of one of his own patients during a phase of intense emotional disturbance. Doubtless other cases could be added, but it is obviously difficult to establish a cause and effect relationship.

Turning to "dynamic" studies (those concerned with the forces at work in the mind of the sufferer), Leigh examines critically the work of French and Alexander, well known to clinicians because of its tentative suggestion, later misquoted as a deliberate conclusion, that asthma is related to a suppressed cry for the mother, from whom there is a fear of separation. Leigh describes this work as an admirable study in speculation from which few facts emerge. He criticizes the work of subsequent writers chiefly because of the subjective nature of the material used to further their studies, for example, the interpretation of play, assumptions that certain behaviour is linked with certain emotions and so on, and the lack of control studies with the use of a statistical approach.

While every pædiatric clinician is familiar with a particular type of mother-child relationship in his asthmatic patients, more research is needed before this can be generally adopted as a major theme. Leigh notes that it is surprising that no "follow-up" studies have been reported by the Chicago school from which the initial work came.

A particularly interesting section of Leigh's review deals with psycho-physiological experimental work, along which lines he anticipates that further advances in the understanding of psychiatric aspects of asthma will be found. He refers in particular to the experiments of Wolf *et alii* which are similar in outline to those which the same workers conducted in regard to gastric function. They found that swelling and congestion of the nasal mucosa occurred when topics distressing to the patient were discussed. Leigh records briefly the results of an investigation of 25 asthmatic patients by discontinuous spectroscopic oximetry during a psychiatric interview. Emotional tension was found to be accompanied by anoxæmia which was relieved by the appropriate motor expression (weeping, laughter) or by asthma. It was considered that in these circumstances the asthmatic attack might be a homœostatic response to relative anoxæmia which in turn could be caused by pent-up emotion.

The section devoted to treatment is, on Leigh's own submission, unsatisfactory. In his opinion no series has been published by a psychiatrist which pays sufficient attention to the vagaries of the natural history of asthma, which includes a control series not treated by psychiatric methods and which embodies a standardized method of treatment, a long-term follow-up and the use of statistical methods. In the absence of such work, it can merely be said that psychotherapy offers encouraging but inconclusive results, that putting the asthmatic child in a boarding

[1] *Internat. Arch. Allergy & Appl. Immunol.*, 1953, Volume IV, Number 4.

school ("environmental manipulation") is very often beneficial, that hypnosis can stop an asthmatic attack and may be worth a trial when other methods fail, that electro-convulsive therapy and insulin shock have been given to asthmatics at least without apparent harm, and that one man has had a leucotomy with diminution in the frequency of his asthmatic attacks and no diminution in his eczema. Such statements are insufficient to support the contention that psychiatric factors are dominant in the production of asthma. In fairness to the psychiatrists, it should be added that Leigh's criticisms are applicable to a considerable number of the papers published by allergists. In entering a plea for thorough critical investigations, Leigh justly observes that the psychiatric literature is stimulating and fertile in ideas, but in his view the concept of a common personality and a common basic problem should be abandoned in favour of the more flexible concept of genetic and constitutional "predisposition" influenced by stimuli of varied provenance. Leigh believes that "predisposition" may be partly explained by further studies of the hereditary factor and of the psycho-physiology of asthma.

At present, it would seem that Laennec expresses quite well the modern physician's outlook on the ætiology of asthma. He lists a number of "causes" of asthma, including emotion, catarrh, emphysema, debility and a "deranged state of the nervous influence, occasioning pulmonary spasm or an increase of the necessity of respiration", but "in fact, I believe there are few cases of asthma owing to any one of these causes; and in old men more particularly, I imagine that several frequently conspire to produce the result". Despite the addition of allergy to the list of causes it is still difficult over a century later to be any more precise.

CHRONIC BRONCHITIS AND ANTIBIOTICS.

CHRONIC BRONCHITIS is a common and crippling disease, but it has been neglected, particularly in relation to infection as a factor in its ætiology and course. No doubt the "familiarity breeds contempt" attitude has played a part in this neglect, but two other reasons suggested by C. H. Stuart-Harris, Margaret Pownall, Cynthia M. Scothorne and Zena Franks[1] are, first, a feeling that such a chronic disease is degenerative rather than infective in origin, and second, past inability to interfere with the course of an infection in a specific manner. However, as they point out, the introduction of antibiotics has now made it possible to alter the symptoms of chronic bronchitis, and the factor of infection has therefore become important. With this in mind, they carried out bacteriological observations upon 113 patients who had chronic bronchitis with or without heart failure and were admitted to hospital between 1949 and 1952. They found that the pneumococcus was a frequent inhabitant of the sputum in all phases of the disease. Other species of potentially pathogenic character were less frequent, but selective media favouring *Hæmophilus influenzæ* were not employed—a significant negative point in view of the observations of later workers. It was also found that influenza virus infection was detected chiefly in relation to the acute exacerbations of chronic bronchitis, but infection was not invariably accompanied by clinical relapse. The distribution of types of pneumococci found in the sputum resembled that found in the naso-pharynx of normal individuals more closely than that found in the sputum in cases of pneumonia. The exact role of these organisms in infection is not easily decided, but Stuart-Harris and his colleagues point out that elimination of the organism is the only safe method of deciding whether or not its presence is harmful. This elimination from the sputum in cases of chronic bronchitis can be achieved with varying degrees of ease by antibiotic treatment. Penicillin is highly effective against the pneumococcus, but somewhat less effective against hæmophilus organisms; it decreases the cough and the purulent character of the sputum, though the sputum rarely dries up. Various antibiotics of the streptomyces family are more regularly inhibitory to hæmophilus organisms. Terramycin frequently brings about a further diminution in the amount of sputum, even after the use of penicillin. The work of other investigators has suggested that the hæmophilus must be eliminated if symptoms are to be relieved, but it is generally agreed that though the bacteria have been reduced to the vanishing point, the patient with chronic bronchitis will again develop bacteria in the sputum as soon as he returns home. Often also, the sputum increases in amount. Stuart-Harris and his colleagues then refer to the distinction between an actuating cause, which persists throughout the course of a disease process, and one which exerts a provocative action, leading to or promoting the development of lesions, but which subsequently disappears from these lesions. An actuating cause of chronic bronchitis has not been described with certainty, but acute respiratory infections of all grades would appear to promote destruction of the defences of the respiratory tract and to add further damage to that already present in the bronchitic subject. Subsequent chronic colonization of the lower part of the respiratory tract, due perhaps to an inability to rid the bronchi of normally inhaled organisms, furnishes a constant source of irritation to the epithelium and frequently causes active inflammatory reaction. The viewpoint thus reached by these investigators is that in cases of chronic bronchitis, there is essentially a failure of defence of the lower part of the respiratory tract against invasion by naso-pharyngeal organisms. The repeated attacks of respiratory viruses, to which we are all subject, may play a large part in bringing about this state of affairs.

This work is considerably amplified and clarified by the reports of other investigators. J. Robert May[1] has shown that the organisms known to be able to cause acute pulmonary infections occur significantly more often in purulent than in mucoid specimens of sputum in cases of chronic bronchitis. To find out if one or more members of the group could cause infections in this condition, as well as in acute pulmonary disease, he investigated the changes in sputum brought about by antibiotics. From this investigation two organisms, *H. influenzæ* and the pneumococcus, seem to be far more important than any others in chronic bronchitis. May concedes that the therapeutic test has only a limited value in this type of disease; but he points out that the repeated observation of the disappearance of pus when *H. influenzæ* and pneumococci are eradicated from the sputum, together with the reappearance of pus when they return, makes the probability of cause and effect a strong one. The part played by bacterial infection in the pathogenesis of chronic bronchitis is not assessed in these investigations. May states that in most cases chemotherapy seems able only to render a purulent sputum mucoid, and patients with mucoid sputum apparently do not benefit from antibacterial treatment. This suggests to him that, in cases of established chronic bronchitis, bacterial infection is a secondary phenomenon. Its importance as a cause of the hypersecretion of mucus, which is apparently of fundamental importance in chronic bronchitis, is not assessed, nor is any attempt made to define the role of viruses. May further states that the organisms of doubtful pathogenicity in the lungs, especially *Streptococcus viridans*, non-hæmolytic streptococci and *Neisseria catarrhalis*, are found almost universally in both purulent and mucoid sputum. The fact that their incidence is the same in the sputum and throats of the same patients suggests that they represent simply a harmless extension of the flora of the upper part of the respiratory tract into a bronchial tree sufficiently damaged to be unable to dispose of them efficiently. The evidence, then, from bacteriological and chemotherapeutic studies suggests that in cases of chronic bronchitis the mucus in the affected parts of the bronchial tree is colonized more or less evenly by organisms from the upper part of the respiratory tract, most of which are non-pathogens. If infection takes place,

[1] *Quart. J. Med.*, April, 1953.

[1] *Lancet*, October 31, 1953.

as manifested by the production of pus, it is usually caused by *H. influenzæ* or by the pneumococcus.

Although these investigations carried out by May were not planned primarily to assess the place of antibiotics in the treatment of chronic bronchitis, he refers to certain observations which seem to bear directly on this matter. Firstly, he points out, many patients feel worse rather than better after chemotherapy owing to the difficulty in expectorating their residual tenacious mucoid sputum. Secondly, the relapse rate, especially of *H. influenzæ* infections, is high, and in some cases the reappearance of pus in the sputum is accompanied by fever and malaise. May considers that although many patients undoubtedly feel much better for some time after chemotherapy, these disadvantages should strike a note of caution on the indiscriminate use of antibiotics in chronic bronchitis. This view is reinforced by the findings of another group of investigators, P. C. Elmes, K. Knox and C. M. Fletcher.[1] They studied the changes in the bacterial flora of the sputum and the development of resistance in a small group of chronic bronchitics who received courses of penicillin, chloramphenicol, aureomycin and sulphadimidine. The broad finding was that though each drug, except sulphadimidine, temporarily reduced bacterial counts and the purulence of the sputum, the clinical effects were slight. Penicillin was effective against most of the bacteria in the sputum; but it allowed, or even encouraged, the emergence of *H. influenzæ* as a dominant organism, and this was found to be associated with increase in the purulence of the sputum, especially during foggy weather. Penicillin is not considered, therefore, to be suitable for continuous prophylaxis throughout the winter, although it may be suitable for administration intermittently at the onset of an acute exacerbation. Chloramphenicol had a surprisingly small effect on the general bacterial flora. It was effective against *H. influenzæ* and has a possible usefulness, but the danger of agranulocytosis following its repeated or prolonged use renders it unsuitable for prophylaxis. Aureomycin was the most effective of the drugs against the whole group of bacterial flora, but it produced resistance in *S. viridans*, and a second course while resistant strains were still present proved less effective than the first. Thus it appears unsuitable for prophylactic use on either a continuous or an intermittent basis. Sulphadimidine had very little effect on the general bacterial flora. Continuous administration in small doses throughout the winter was found to have no prophylactic effect against winter exacerbations of bronchitis in cases of pneumonokoniosis. Larger doses could hardly be used without risk of toxic effects. Elmes, Knox and Fletcher suggest that intermittent administration may well be of value against exacerbations due to *S. pneumoniæ*, but until the frequency is known with which this organism rather than *H. influenzæ* and the other "denizens" of the sputum are responsible for the exacerbation, its usefulness cannot be forecast. The conclusion reached from this study is that none of the drugs used would be suitable for prophylaxis of acute exacerbations of chronic bronchitis. The requirements of a drug for this purpose are that it should be cheap, free from toxic effects, effective against the whole range of bacteria responsible for chronic bronchitis, and not likely to impart acquired resistance. Such a drug has not yet been found amongst those tested; but, as Elmes, Knox and Fletcher point out, if it became available, an enormous amount of disability in men of working age might be prevented.

[1] *Ibidem.*

TUBERCULOSIS IN SOUTH AUSTRALIA.

IN the annual report of the Department of Public Health and the Central Board of Health of South Australia for the year ended December 31, 1952, some interesting facts are given in the section dealing with tuberculosis. There has been a substantial decrease in the mortality from tuberculosis during the year under review. The tuberculosis death rate of 13·3 for all forms of tuberculosis per 100,000 of population and of 12·1 per 100,000 for pulmonary tuberculosis are the lowest on record for the State. The death rate for all forms of tuberculosis shows a decrease of 20·4% compared with that of 1951 and the pulmonary death rate has fallen by 14·9% in the same time. The number of cases reported has, on the other hand, shown an increase compared with the previous year, and the number has risen from 376 to 416. The increase, it is stated, is a reflection of the increased attendances at the Chest Clinics and a more complete examination of contacts of known cases with an intensification of X-ray surveys. Compulsory X-ray surveys have been introduced and have been conducted by two photofluorographic units operating as before, one in the metropolitan area and one in the country. The city unit has made 16,984 examinations; 341 persons were marked for further investigation owing to suspicion of tuberculosis, and 165 for further investigation though tuberculosis was not suspected. The country unit has made 20,623 examinations; 221 persons have been marked for further investigation because tuberculosis was suspected, and 177 for further investigation though tuberculosis was not suspected. The two significant points which have emerged from these compulsory surveys are first, that the numbers of new cases have shown a slight but definite increase compared with the results in previous voluntary surveys, and secondly, that the vast number of abnormalities found are in the higher age group. For example, in the university survey of 903 persons aged fifteen to nineteen years, 0·35% manifested abnormalities, while of 114 persons aged from forty-five to sixty-four years, 7·9% manifested abnormalities. Special attention has therefore been paid to higher age groups, both in general and in contact surveys. The tuberculosis allowance is mentioned. Certification of eligibility and periodic review of eligibility for the tuberculosis allowance remains one of the major tasks of the Tuberculosis Section of the Department. The allowance is more liberal than that of other service benefits. In South Australia the allowance is undoubtedly succeeding in its aim, but the necessity for frequent review imposes a great strain on the staff. The greatest expansion of activities in the prevention of tuberculosis in 1952 has been the introduction of B.C.G. vaccination for seventh grade school children and for national service trainees. (The vaccination of contacts, medical students, nurses and some others is a function of the Chest Clinics of the Hospitals Department and is recorded elsewhere.) National service trainees to the number of 2212 were tested by tuberculin. A positive reaction was given by 469, or 21·2%. The number of trainees vaccinated with B.C.G. was 1743. The seventh grade school children tested by tuberculin were 3235, and of these, 343 or 10·6% gave a positive reaction. Of those who failed to react, 2792 were vaccinated with B.C.G. Attention is drawn to the variation in the percentage of Mantoux-positive children among those born in Australia and among those born elsewhere; of the Australian-born children 8·5% were tuberculin positive, and the number of children born elsewhere who were tuberculin-positive was 39·4%. It is expected that a considerably larger number of children will be vaccinated in the coming year.

The statement is made that the problems of correlating the tuberculosis work in the Public Health and Hospitals Department remains a difficult one. Duplication of work and correspondence will remain until the administrative work can be carried out in the same building as the Chest Clinic. The report of the work of the Chest Clinic is not included in the present document. Presumably the results of treatment are recorded in the report of that Clinic. This is a pity, for one report is incomplete without the other. It is to be presumed that in the report of the Chest Clinic some mention will be made of the magnificent work which is being carried out at "Cowan Building", the Rehabilitation Centre of the South Australian Tuberculosis Association, which was described in this journal in the issue of February 10, 1951.

Abstracts from Medical Literature.

MEDICINE.

The Effect of Pneumoperitoneum on the Heart and Lungs.

R. C. KORY *et alii* (*Dis. Chest*, June, 1953) have studied the effect of pneumoperitoneum on the function of the heart and lungs. They found that pneumoperitoneum caused a decrease in total lung volume primarily by virtue of a reduction in residual air with little or no change in vital capacity. The arterial oxygen saturation and arterial carbon dioxide content were unaffected. Cardiac output showed a very slight decline. In the presence of emphysema the pneumoperitoneum sometimes caused striking improvement in cardio-pulmonary function, associated with increased inspiratory capacity, reduction in residual air, increased arterial oxygen saturation, decreased carbon dioxide retention and a fall in the cardiac output. One patient with pulmonary hypertension demonstrated a reduction in the pulmonary artery pressure.

Objective Auscultation of the Heart.

A. BRISKIER (*Am. Heart J.*, June, 1953) describes an apparatus for making a permanent audible and visible record of the cardiac phenomena, the audio-visocardiogram. The apparatus consists of an electrocardiograph, a phonostethograph and an electromagnetic tape recorder combined in one unit. The sound tape is detachable from the permanent record and can be removed, played back and filed again at any time.

Excretion of Sodium-Retaining Substances in Heart Failure.

B. SINGER AND J. WENER (*Am. Heart J.*, June, 1953) have found that patients with congestive heart failure excrete in the urine excessive quantities of salt-retaining substances resembling in their action desoxycorticosterone acetate. The finding was made by assaying the excretion of radioactive sodium by supradrenalectomized rats after the rats had received an injection of urine from the patients or a control injection.

Electroplexy in Tuberculous Patients.

M. SILVERMAN (*Brit. J. Tuberc. & Dis. Chest*, July, 1953) reports two cases of depressive psychosis in tuberculous patients, who were treated by electroplexy, modified by the use of relaxing agents, while streptomycin and sodium para-aminosalicylate were given to depress bacterial activity. In each case the patient was favourably affected in regard to the psychosis and not adversely affected in regard to the tuberculous disease.

Cancer of Thoracic Stomach.

D. ROBB (*J. Thoracic Surg.*, May, 1953) reports three cases of malignant disease encountered during the surgical treatment of 70 patients with hiatus hernia and thoracic stomach. One was an adenocarcinoma and one a fibrosarcoma of the œsophagus, and one was an adenocarcinoma of the stomach. The author cites a previous report of two cases of adenocarcinoma of the stomach in which the stomach was lying partly in the thorax.

Toxic Effects of Para-Aminosalicylates (PAS).

J. EVANS (*Brit. J. Tuberc. & Dis. Chest*, April, 1953) reviews the toxic effects of para-aminosalicylates (PAS). These include skin eruptions, albuminuria, hæmaturia, anuria, renal glycosuria, asthma, intractable cough, laryngeal stridor, pharyngitis, inflammation of the salivary glands, hypokalæmia (with palsy, tetany and cardiac arrhythmia), purpura, lymphoglandular enlargement, leucopenia, anæmia, leucocytosis (with a leuchæmoid blood picture in one case described by the author) and jaundice. In addition to these toxic effects rather more than half the patients receiving the drug complained of gastro-intestinal symptoms. Five fatalities due to the drug have been reported.

The "Opening Snap" in Mitral Stenosis.

P. MOUNSEY (*Brit. Heart J.*, April, 1953) found that the "opening snap" of the mitral valve was recorded by the phonocardiogram in 32 out of 33 cases of mitral stenosis, though it was inaudible in four of these. It was usually loudest in the area just above and medial to the left breast, whereas the second component of a split second sound was always loudest in the pulmonary area. As both a split second sound and the opening snap are nearly always present in the same patient their differentiation is relatively easy. The physiological third heart sound was lower in pitch than the opening snap and occurred a little later in diastole; it is frequently present in mitral valvular incompetence where the left ventricle fills rapidly. Absence or diminution in intensity of the opening snap is associated with gross calcification of the mitral valve.

Cation-Exchange Resin in the Treatment of Œdema.

A. A. F. PEEL AND T. SEMPLE (*Brit. Heart J.*, July, 1953) discuss the treatment of cardiac œdema with a balanced ammonium-potassium carboxylic resin. They state that biochemical control is essential in the early stages of treatment, especially for patients with renal impairment and for those who have been receiving diets of low sodium content or mercurial diuretics—such patients may have abnormal blood electrolyte levels, which may be corrected or aggravated by resin therapy. Subject to biochemical control, the resin may be used as a substitute for a diet of low sodium content or to reinforce its effect. When it is given in addition to a diet of low sodium content, the best result is obtained from repeated short courses of the resin. As resin therapy tends to produce hyperchlorræmia and a diet of low sodium content tends to produce hypochlorræmia, patients intolerant of one of these forms of treatment may prove ideal for the other. Undesirable side-effects appeared in half the patients treated by the authors, including hyperchlorræmia with anorexia and depression, hyperkalæmia with diarrhœa, hypokalæmia with mental confusion, and digitalis intoxication. Apart from the more serious side-effects, most of the patients complained that the resin left a lingering sticky feeling on the lips, tongue and palate, and many preferred a dietetic regimen to the resin.

Clinical Use of Triethylene Melamine.

WILLIAM H. BOND, ROBERT J. ROHN, RICHARD W. DYKE AND PAUL J. FOUTS (*Arch. Int. Med.*, May, 1953) discuss the clinical use of triethylene melamine. Since 1950, the authors have treated 75 patients with this drug; the majority of the patients were suffering from leuchæmia or malignant lymphoma. An analysis of the results of treatment is presented. In all instances, the diagnosis was established by peripheral blood and bone marrow examinations, and/or lymph node or appropriate tissue biopsy studies. During the first several months' experience in the use of triethylene melamine, all patients were admitted to hospital. Later, patients were treated on both an in-patient and an out-patient basis. At all times, careful complete evaluation of the hæmatological status was made at frequent intervals. The drug was administered orally to all patients, and for the great majority five milligramme tablets were used. For those who experienced considerable nausea, one milligramme tablets were given at more frequent intervals. Also, one milligramme tablets were used for most cases of acute leuchæmia in which rapid cellular lysis might prove embarrassing. Seventy-seven disease entities in 75 patients were treated, and chronic myelogenous leuchæmia and chronic lymphatic leuchæmia were the diseases most effectively controlled by the drug. Secondary hæmolytic anæmias were temporarily controlled with the drug in two cases, and further clinical trial seems indicated. In some cases of subacute myelogenous and monocytic leuchæmia, transitory subjective improvement and partial hæmatological remissions were observed. No significant hæmatological response was observed in four adults with leuco-lymphosarcoma. In widely disseminated advanced Hodgkin's disease, therapeutic benefits with triethylene melamine were not as gratifying as those reported by others. No significant benefits were observed in patients with a small miscellaneous group of diseases, which included extramedullary lymphosarcoma, fibrosarcoma, Ewing's tumour, malignant melanoma, sarcoidosis and *polycythæmia rubra*, resistant to radioactive phosphorus. Dosage schedules varied widely according to the disease; toxic reactions were minimal and consisted principally of anorexia, nausea and vomiting. Excessive depression of the hæmatopoietic system occurred in seven cases. The authors consider that triethylene melamine offers a valuable form of adjunctive therapy in the treatment of some diseases of the reticulo-endothelial system.

Late Results of Treatment of Thyrotoxicosis with Thiouracil Compounds.

DORIS I. MANSON (*Edinburgh M. J.*, July, 1953) analyses the results of treatment of thyrotoxicosis with thiouracil compounds. The results are based upon the study of 112 patients

who were observed from 1943 till 1952. Thiouracil, methyl-thiouracil and propyl-thiouracil were the drugs used, and were administered initially in daily doses of 400 to 600 milligrammes, 200 to 400 milligrammes and 100 to 400 milligrammes, respectively. Maintenance doses were reduced to 100 milligrammes, 50 to 25 milligrammes and 25 milligrammes, respectively, for the three drugs. Taking into account the results in this series of cases and in published series, the author suggests that subtotal thyroidectomy should be recommended in the presence of the following conditions: (i) tracheal compression and retrosternal extension, (ii) nodular goitre and all types of secondary thyrotoxicosis, (iii) large diffuse hyperplastic goitre, particularly when present for some months, (iv) severe degree of thyrotoxicosis (basal metabolic rate greater than +60%). In the present series, if the patients who had secondary thyrotoxicosis, large hyperplastic goitre and severe degree of toxicity are excluded, the remission rate after one course of thiouracil is 71%. Apart from this, a remission rate of 61% was observed. Age, sex and duration of symptoms did not influence the result of treatment; but severe thyrotoxicosis, large goitre and nodular goitre had an adverse effect. It was found that treatment was best continued for at least nine months, and that the majority of those who relapsed after cessation of therapy did so within six months.

Topical Applications in Chronic Rheumatic Diseases.

R. A. MANNING AND H. G. BRUGOCH (*Connecticut M. J.*, June, 1953) report a controlled evaluation of the local effects of a proprietary liniment and a proprietary ointment containing certain counter-irritants and analgesics in a preliminary short-term study on 148 patients with a variety of rheumatic diseases. In 120 of 146 tests with these agents, improved function was demonstrated, in the form of greater muscular strength or increased range of motion; this compares favourably with improvement in 61 of 105 tests with placebos. Subjective improvement was significantly commoner in the treated group than in the controls. The authors state that although the changes in skin temperature observed after the use of the medicated preparations and the control substances varied directly with changes in function, further evidence is needed to establish a causal relationship. It is concluded that topical treatment with the analgesic preparations used in this study seems to afford a safe and readily applicable aid to physical therapy. It does not obviate the need for systemic anti-rheumatic treatment in suitable cases. It facilitates the control of rheumatic pain and disability, particularly under conditions of domiciliary care.

Arterial Hypertension.

R. M. HILL (*Edinburgh M. J.*, July, 1953) discusses arterial hypertension and makes some observations on the treatment of this disease based upon observation of a series of 33 patients for from three months to more than four years after sympathectomy. He states that arterial hypertension is a syndrome based on an error of the adrenal and its relatives in the endocrine system. The process is essentially an affection of the arteriolar system, varying in degree from slight intimal cellular increase to hyaline necrosis, evident on retinoscopy and examination of renal biopsy sections. The rate of development of the process alone determines the qualification benign or malignant. The causes are complex; the place of the adrenal medulla, the pituitary, the adrenal cortex and the kidney in the production of vasopressor agents is not yet clear, but it may well be that some of the steroids of the adrenal cortex play a major part. It is suggested that the effects of sympathectomy on the adrenals is of first importance. In view of the natural history of this disorder and the effect of general care and guidance in the majority of mild and transient cases, it appears rational to employ sympathectomy in certain cases until the advent of some substance with specific action. Operative treatment is indicated in cases of malignant hypertension, especially in young subjects, in cases not controlled by conservative measures, and in cases in which the patients are unable to maintain their treatment. It has been shown that symptoms may be relieved, that pathological changes are reversible, and that patients may be restored to well-being—for how long and at what level, only long-term studies may determine.

"Butazolidin."

J. P. CURRIE, R. A. PEEBLES BROWN AND G. WILL (*Ann. Rheumat. Dis.*, June, 1953) report their experiences with the use of "Butazolidin" in the treatment of 424 subjects of rheumatoid arthritis at the Rheumatism Clinic, Glasgow Royal Infirmary. They review the pharmacology of the drug and state that rapid and substantial relief is given in over 90% of cases. Toxic effects occurred in 4·7% of cases and were mild—nausea, rash, œdema, albuminuria, stomatitis, tachycardia and tingling of the toes. The authors advocate moderation in dosage, starting with 200 milligrammes four times on the first day and reducing this until the patients are taking 200 milligrammes daily from the sixth day. The maintenance dose is then adjusted according to the clinical results or the blood level.

Hydrocortisone for Rheumatoid Arthritis.

EDWARD W. BOLAND (*Ann. Rheumat. Dis.*, June, 1953) states that hydrocortisone (Kendall's compound F) given by mouth is very much more potent than cortisone acetate in controlling the inflammatory aspects of rheumatoid arthritis and is much less toxic.

Cortisone and Rheumatic Heart Disease.

A. L. JOHNSON AND C. FERENCZ (*New England J. Med.*, May 14, 1953) discuss the effect of cortisone therapy on the incidence of rheumatic heart disease. They compare 100 patients treated with cortisone (mainly) and ACTH (in a few cases) with 80 patients treated prior to the introduction of these drugs. They conclude that cortisone frequently has a very beneficial effect in cases of rheumatic carditis and that the patients appear to be much improved by this treatment, but that in the long run the patients seem to develop cardiac abnormalities just as frequently under cortisone as under salicylate treatment. The after effects were apparently much the same with either method of treatment, and the recurrences were not affected by such treatment. Generally, although cortisone produced immediate benefit in many cases, the general effect was not modified to any extent. The dosage of cortisone was usually 200 milligrammes for two days and 100 to 150 milligrammes for twenty-eight days. ACTH was given in doses of 40 to 60 milligrammes intramuscularly for seven to forty days. There was apparently no significant difference in the incidence of heart disease after the advent of cortisone compared with that before cortisone was used.

Pulmonary Emphysema.

A. A. ABBOTT *et alii* (*Thorax*, June, 1953) describe a new approach to pulmonary emphysema. They state that tobacco and lung suppuration are the principal causes of this condition. Bronchospasm is stated to have been evident in many patients, as indicated by wheezing, response to bronchodilating drugs and bronchoscopic findings. Aminophylline, adrenaline and "Banthine" are described as having been employed with benefit. The authors have divided emphysema into certain types, and have carried out surgical procedures such as surgical removal of bullæ, sympathectomy and transection of the vagus. They state that considerable success has been attained in all except "desperate" cases.

Isolation of a Virus as the Cause of Behcet's Disease.

F. NEDECT SEZER (*Am. J. Ophth.*, March, 1953) describes the signs of Behcet's disease and describes the isolation of a virus in three cases. He states that there are three basic and invariable signs: iridocyclitis with hypopyon, aphthæ in the mucosa of the mouth and ulceration of the sexual organs. The most important characteristic of the disease is its recurrence with the appearance of all three symptoms, either together or one after the other. As the disease progresses, the intervals between the attacks lengthen until finally there are no further attacks. The age of onset of the disease is usually between fifteen and forty years, and most victims are males. The author studied 30 cases and attempted to produce an experimental disease in the eyes of rabbits with material from the anterior chamber or aphthæ without success. Three cases were studied in which the vitreous was used from one affected subject and subretinal serous fluid from two others, and from this fluid the author was able to isolate a virus and also to produce the disease by passage through laboratory animals. Failure to isolate a virus in the past was due to the fact that only aqueous and exudate from aphthæ were used. The virus multiplied on the chorio-allantoic membrane of the developing embryo, and killed guinea-pigs by causing hæmorrhagic lobar pneumonia. The virus, as measured under the electron microscope, has a diameter of 100 millimicrons. The author is able to conclude that the syndrome is an independent disease due to a filtrable, neurotropic virus.

Special Articles for the Clinician.

(CONTRIBUTED BY REQUEST.)

XC.

THE MANAGEMENT OF BLADDER NECK OBSTRUCTION.

THE management of bladder neck obstruction necessarily varies with the pathology of the obstructive lesion, which in the overwhelming preponderance of cases is of one of three types: (i) adenomatous, (ii) malignant, (iii) fibrotic; and any of these three types may coexist.

Adenomatous Obstruction.

Adenomatous bladder neck obstruction is commonly referred to as benign prostatic hypertrophy. The exact pathology has long been the subject of investigation and controversy, but from the clinical point of view it is relatively unimportant, as the lesion behaves like an adenoma, either single or multiple, and is treated as such. It commences either in the urethral glands or in the prostatic glands immediately adjacent to the urethral lumen, and results in a growing mass of tissue of glandular structure, which grows upwards, or laterally, or in both directions. If it grows upwards, it may, depending on its point of origin, grow up through the internal sphincter or subtrigonally; while if it grows laterally, it pushes out and compresses the previously normal prostatic tissue, which is otherwise unaffected by the disease process. Finally, the true prostate becomes a thin shell of tissue, which surrounds the "hypertrophy" and is commonly termed the false capsule. Between this and the "hypertrophy" is a comparatively avascular line of cleavage, and it is along this plane that the finger sweeps in the course of a "prostatectomy", which in view of the foregoing considerations is obviously not a prostatectomy at all, but simply a removal of the obstructive adenomatous tissue, the true prostate being left behind. Obviously again, a "prostatectomy" on this basis does not confer permanent immunity from recurrence or prevent the development in future years of prostatic malignant disease.

Treatment.

Non-surgical treatment has little or no place in the management of the type of lesion under discussion. The obstruction is a mechanical one, and is not amenable to treatment other than of a mechanical order. Testosterone, although used on occasions, has been investigated and has been found of equal value to distilled water used in a comparable series of cases. Stilbœstrol also has no place. Practically all that one can do from a non-surgical viewpoint is to tell the patient to avoid retention of urine by (*a*) avoiding alcohol and (*b*) passing urine any time he experiences the desire to do so, irrespective of social or other considerations.

Surgical treatment entails prostatectomy by any of the adequate modern techniques. These are various—suprapubic prostatectomy with drainage, Harris prostatectomy, Wilson-Hey prostatectomy, retropubic, perineal, transurethral and so on. Provided that one offers the patient, as one can, a safe operation followed by a normal expectancy of fourteen days or less in hospital, the type of prostatectomy is of little importance. All are normally followed by good results, all are very occasionally followed by difficult or distressing complications, and all inevitably entail a definite though small mortality. In this connexion the term "transurethral prostatectomy" is used advisedly. The operation of "canalization of the posterior urethra", more commonly known as "nipping a little bit off", has been abundantly proved to be worse than useless and was discarded almost as soon as it was introduced in the middle 1930's. One is often asked whether a case is suitable for transurethral operation, and one answers "yes" or "no" as the case may be. The fact is, however, that practically all adenomatous prostates can be dealt with by this method, and the question therefore is not so much of the suitability of the patient as of the suitability of the surgeon. Some surgeons, but they are relatively few, have the skill, patience and experience that enable them to resect practically all adenomatous prostates that come their way. Others lack one or more of these qualities and therefore find the operation less widely applicable. Others again consider that a forty-minute open prostatectomy is preferable to a sixty-minute operation by the transurethral route. But whatever method is best suited to the requirements of the patient and the experience, temperament and convictions of the surgeon, the results on both a short-term and a long-term basis are roughly equivalent.

Indications for Operation.

At one end of the scale is the group of patients, with retention of urine despite repeated catheterization, in whom operation obviously has to be carried out at whatever reasonable risk. At the other end is the group in which the symptoms constitute a mild annoyance, insufficient in the patient's opinion to justify surgery, and in this group operation is contraindicated. It has to be remembered that prostatectomy is not invariably followed by entirely normal micturition, and a patient who has to rise once at night will not be particularly grateful if after operation he has to rise twice.

For the majority of patients, who occupy a position intermediate between these two groups, the operation is one of reasonable election. One must weigh the various contingent circumstances—the patient's age, family tree, expectation of life and general physical condition—against the severity and degree of progression of his symptoms, and decide whether to advise operation or advise the patient that he can carry on if he prefers in reasonable safety. Most patients can reasonably be left to make up their own minds, and it must not be forgotten that the terminal uræmia so stressed by the text-books is a comparative rarity. Most patients will be forced into operation by the severity of their symptoms long before it develops, and it is surgically wrong to advise a patient in the early stages of prostatism that he must undergo operation to save him from developments that in the vast majority of cases will never occur.

Malignant Obstruction.

Carcinoma of the prostate normally starts in the posterior lamella, and it is generally felt that by the time it extends to the urethra and causes symptoms it has become inoperable. At the same time, an increasing number of American urologists are carrying out total perineal prostatectomy for extremely early malignant changes, asymptomatic, accidentally discovered and proven by frozen section examination at the time of operation; while some of the British school are carrying out total retropubic prostatectomy for some of the malignant changes that have reached the stage of becoming clinically obvious. Except as employed as mentioned above—namely, to be followed by total prostatectomy if carcinoma is present—perineal biopsy is considered by the vast majority of urologists to have no place in the management of bladder neck obstruction. For the most part, however, treatment is hormonal, by either the free stilbœstrol or the rather expensive TACE. Orchidectomy, of course, is also a recognized mode of treatment. Statistically, orchidectomy followed by stilbœstrol results in a life expectancy slightly longer than the average of that which follows either of these methods of treatment used alone. However, most urologists prefer to avoid it, as to the patient it is a major procedure, the necessity for which takes a lot of explaining. Whether it is better to have a contented patient who thinks he has been cured by tablets, or an orchidectomized patient who knows he has cancer, is a question that each urologist decides for himself.

If malignant change is suspected, stilbœstrol is always worth trying on a short-term basis; and response, if it occurs, is immediate and dramatic. If the patient fails to respond to a dosage of 15 milligrammes daily within two or three days, (i) the prostate is not malignant, or (ii) the malignant condition is stilbœstrol-resistant, or (iii) malignant change is present in the posterior part of the gland, but the obstruction causing the symptoms is adenomatous. Response to stilbœstrol is not of indefinite duration. It may last till some other disease terminates the patient's life, or it may cease after an unpredictable number of months or years. It follows that when this stage is reached, recourse has to be had to pre-hormonal methods of treatment—namely, transurethral resection and deep X-ray therapy.

Fibrotic Obstruction.

Fibrotic obstruction is due to what is commonly known as the small fibrous prostate. The prostate is normal on rectal examination, and there is no adenoma or plane of cleavage. "Prostatectomy" therefore is not feasible. Suprapubic excision of the fibrous obstruction can be carried out, but transurethral resection is generally considered preferable. Total retropubic prostatectomy has been carried out for this condition, but few self-respecting urologists would consider it.

Acute Retention of Urine.

The customary treatment for acute retention of urine is catheterization, followed, if the patient is still unable to pass urine, by further catheterization and prostatectomy in due course. However, a small but increasing number of urologists are convinced that immediate prostatectomy is the procedure indicated. The results quoted are satisfactory, but this approach will not become generally accepted until such time—if ever—as hospitals are prepared to accord to patients in this category the same degree of priority as they extend to acute appendicitis or perforated ulcers. In the meantime the general practitioner has to treat the retention and not the prostate and make his patient comfortable, for which a coudé catheter of the Tiemann type is essential. If the patient's bladder cannot be catheterized, immediate prostatectomy—all things being equal—is becoming increasingly regarded as preferable to two-stage operation.

Chronic Retention of Urine.

With chronic retention of urine, although the patient has a full bladder, he has as a general rule been carrying on with it for weeks or months. He is in chronic and not in acute distress, and there is no immediate indication to relieve it. In other words, he should most definitely not have his bladder catheterized, as such patients are a particularly easy prey to infection. He should be left severely alone until such time as he can be admitted to hospital and have his obstructive lesion removed, either immediately after admission or after preliminary treatment, depending on the exigencies of the individual case and the feelings of the individual surgeon.

M. S. S. EARLAM,
Sydney.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

INOCULATION OF RABBITS WITH SYPHILIS.

[*The Australian Medical Journal*, May, 1869.][1]

Some persons in the Western District (Vic.) have been inoculating the rabbits with the syphilitic virus with the view to get rid of the nuisance of these animals. The act is as disgusting as it is useless for the purpose intended, and merits the strongest reprobation.

Special Correspondence.

LONDON LETTER.

By OUR SPECIAL REPRESENTATIVE.

THE summer months in England were once considered to be deficient in news and newspapers relied on filling their columns with items not likely to disturb the equanimity of the Englishman on holiday.

Nowadays the Englishman, if he does read a newspaper on holiday, may find his peace of mind disturbed by alarming situations due to the constant state of tension in the world. There must be few Englishmen (or Welshmen or Scotsmen) who do not have an annual holiday with pay, and most of them want to spend it with their wives and children. Hence the most popular time for the holiday is the month of August which corresponds to the children's summer recess from school.

The doctor with a family also finds August a convenient month to be on vacation. The general practitioner must arrange a *locum tenens*, but with the increase of group practice, the partners usually relieve each other in turn. In the Hospital Service, the consultants, who are entitled to six weeks' annual leave with pay and who also maybe are men with families, depart for the sea and countryside, arranging with a colleague to carry on in their absence. Thus, there is a general dearth of consultants in August.

In August, too, there are, as a rule, no regular meetings of committees or medical societies. The summer months do, however, provide the opportunity for medical men to gather in conference on many aspects of their work. Conferences on medical education and medical librarianship and a conference of the Pharmaceutical Society are among those which have been held in London recently.

First International Conference on Medical Education.

The aim of the conference on medical education was to try to discover how best to teach young men and women who are to be the doctors of the future. It was attended by some 400 delegates from 20 countries, and arrangements for the simultaneous translation of the speeches in English, French and Spanish were provided. The conference was distressed to learn of the death of Dr. René Sand, Professor of Social Medicine at Brussels University, who was to have spoken. The conference was opened by Miss Hornsby Smith, Parliamentary Secretary to the Minister of Health, and the President, Sir Lionel Whitby, Vice-Chancellor of the University of Cambridge, broadly surveyed the scope of the conference and spoke of the qualities required of the ideal medical student. Knowledge had so accumulated today as to demand early specialization and made it impossible for a man to be complete in all his subjects. There was need for more intergration in the curriculum. He favoured the tutorial system of teaching and felt that the properly chosen medical tutor could contribute much to real integration and do away with piecemeal instruction as well as disproportionate departmental emphasis.

The conference divided into four sections to make a detailed examination of the medical curriculum. Some forthright criticisms were evoked concerning the quality of would-be doctors, the trend of specialization, the alleged neglect of preventive medicine and the slavish following of the text-book. The Professor of Medicine of the University of Birmingham spoke of the criticism sometimes levelled at medical schools that they were not turning out "practical men", by which was often meant the sort of man who could empty a waiting room of sixty patients in an hour. Far more important was the capacity to think straight, to know how to make a diagnosis, to know good evidence from bad and to recognize an unusual situation. Medicine would be followed with advantage only by those above average in intelligence and character, and circumstances of birth, social rank or material endowment should play no great part in recruitment. Dr. Denis Brinton, of St. Mary's Hospital, London, spoke of the diminished academic and personal standards of those entering medicine today. There were today certain powerful but undistinguished motives for becoming a doctor. Parents felt that the terms and conditions of the National Health Service increased the sense of security for a son or daughter entering medicine. Dr. Oliver Cope, Associate Professor of Surgery, Harvard Medical School, United States of America, referred to a "helter skelter" trend towards specialization in medicine, teaching, research and practice. Air Vice-Marshal Sir Alan Rook, Senior Health Officer, University of Cambridge, said that unfortunately preventive medicine made no great appeal to the average doctor. Notwithstanding the economic and practical value of the prevention of disease, its humdrum routine compared unfavourably with the colour and drama of clinical medicine and surgery. The present teaching methods were unlikely to impress medical students with the importance of disease prevention. The average doctor left hospital having heard little about preventive medicine and often felt that however worthy, it was a subject which hardly concerned him. The part to be played by the humanities in the education of the doctor was discussed by another section of the conference under the title "General Education in an Age of Science", and there was marked unanimity that science, particularly medical science, should not be the whole of a doctor's heart, mind and soul. Mr. T. E. B. Howarth, a Master of Winchester School, remarked that if ours was an age of science, it was also an age of human beings and the problem was not only to ensure that science directed humanity but to enable humanity to direct science. He asked whether prospective medical students knew enough about the human to balance their extensive knowledge of the sub-human. In England, a schoolboy began preparation for the medical profession as early as fifteen or sixteen years of age to such an extent that not more than one-quarter of his school studies would be devoted to subjects other than biology, physics, chemistry and mathematics, which left a very narrow margin for general education.

[1] From the original in the Mitchell Library, Sydney.

Speaking of the causes of breakdowns and failures among university students, the Tutor of St. Catherine's College, Cambridge, ascribed many of the breakdowns to the forcing of students into work against their true inclination and training. This often applied to the medical student who was forced into medicine to take on his father's practice. Frustration, unhappiness and waste were caused by forcing students into university courses when they had not the intelligence, training, personality or mental fibre to meet the demand of such an education. Six hours of really hard work was the most that could be absorbed and understood profitably by a student in one day. More than that tended to increase the use of drugs, for example, "Benzedrine", which was worse than useless. A real trouble, often unsuspected, was severe eye strain. One of the more important causes of failure was the effect of a class conflict on the family of a student who had won a university education. Acquired standards of living, taste and outlook widened the gap between his family and himself. The family, torn by pride and irritation at the waste of money, tended to emphasize the burden of the student's obligations to do well and hence his fear of failure. Sex, in his opinion, was not an important cause of failure. Sometimes an unfortunate student might take refuge in drink or drugs, but most of these students recovered in course of time. University teachers could do something to ensure that only intellectually suitable material was admitted and develop in themselves and their students a sane attitude towards examinations.

British Pharmaceutical Conference.

Pharmacists from all over Britain and representatives from 25 other countries have also met in conference this summer and discussed among other important matters the debatable question of English *versus* Latin in the wording of prescriptions. The arguments for English were presented by Professor A. D. MacDonald, Professor of Pharmacology in the University of Manchester, who claimed that the Latin used was not Latin at all, but a clumsy mixture of improvisation, a system of shorthand based on Latin. In any case it could not be assumed that the newly qualified doctor had a working knowledge of Latin, as in most examinations Latin was no longer compulsory for matriculation. Prescriptions might just as well be written in English, and the British Pharmacopœia gave English titles pride of place. He asked: "Are we ashamed of the therapy we dispense or prescribe?" The arguments for the retention of Latin were that Latin was precise in meaning and not subject to change, whereas the English tongue was capable of more than one meaning and had changed almost out of recognition in a few centuries. Latin was understood by educated men throughout the world and prescriptions written in almost any country could be deciphered by a pharmacist. It was undesirable that patients should, on all occasions, be aware of the type and nature of drugs prescribed for their use.

An announcement was made by the chairman of the conference, Dr. G. R. Boyes, of a new and improved compound of insulin, insulin zinc suspension, which would keep the average diabetic in control with one injection daily.

The Association of British Pharmaceutical Industry has taken certain steps which may eventually lead to a change in the prescription of drugs by medical practitioners. It has recommended its members to use metric weights and measures in wholesale trading, and the Ministry of Health has already begun the supply of drugs in bulk to hospitals in metric weights and measures. The next step may be the conversion of medical prescribing to the metric system and a break with tradition which is likely to arouse considerable controversy. The question has become more acute since the development of the newer drugs, which are prepared in metric doses. The advocates of the metric system point to the difficulties encountered by the medical student, who in his early years of study uses the metric system for the basic sciences, and in his clinical years is taught to prescribe in the archaic Imperial system of weights and measures. So much for the logical approach, but the opponents of change have much on their side. There is, for example, the practical difficulty of expressing metric measurements in terms of some domestic equivalent, to which the Imperial system is more closely related. Even in France, the home of logic, a doctor's prescription is likely to end with the instruction: "A coffee spoonful three times a day."

Although the British Government has been a member of the Metric Convention since 1885, it is still not prepared to recommend any official change from the Imperial system to metric, in spite of the strongly worded recommendations of the Hodgson Committee in May, 1951. What is most needed is not the universal adoption of the metric system, but the development of an agreed international system of weights and measures. In this connexion, there is the apposite remark of an American engineer at an international conference: "Your metre, my foot."

Any change in the system of prescribing would bear hardly on the older generation of doctors and it might take twenty years to effect a change. Some protagonists suggest an "overnight" change and quote the change in the helm orders of ships some years ago which was achieved in this way without any confusion or mishap. The case for the metric system in medicine stands or falls by a satisfactory answer to the question: "How is the dose to be prescribed?"

The International Conference of Medical Librarianship.

Medical librarians from thirty countries assembled recently in London to attend the first International Conference on Medical Librarianship. The President of the Conference, Sir Cecil Wakeley, P.R.C.S., spoke on the highly specialized nature of the subject, and of its increasing value in the complexity of modern medicine, and the bulk and variety of medical literature. Some idea of this mass of literature could be gained by the exhibition on view of some 2500 journals. The medical librarian was needed to reduce this formidable mass to some sort of order; he hoped that it would be possible for each country to produce a current index of its own medical literature, to be collected and reissued by some international agency such as the World Health Organization or UNESCO.

Britain was one of the few countries which had a qualifying examination in medical librarianship and the average period of study from registration to final examination was four years.

Correspondence.

COMFORT IN CALLIPERS.

SIR: Might I draw the attention of your readers to the letter by Dr. H. L. Rogerson, of Norfolk, England, on page 337 of the *British Medical Journal* of August 8, 1953? Like Dr. Rogerson, since being a calliper user myself, I have been appalled with the poor standard of workmanship and cumbersome article which is turned out by the majority of splint-makers in this State and inflicted on the poor unfortunate patients. The chief faults are inferior material, shoddy workmanship, the weight of the article and the complete disregard for accurate fitting of the limb. Both doctors and splint-makers seem to lose sight of the fact that the only way to walk in a walking calliper is for the knee to be in complete extension, a support if necessary, to prevent flexion and over-hypoextension. As poliomyelitis seems to have come to stay, might I make an appeal to our colleagues in general, and particularly our orthopædic ones, for more attention to the design, manufacture and comfort of callipers for the betterment of the patient.

Yours, etc.,

Gerrale Street,
Cronulla,
New South Wales.
November 5, 1953.

A. M. MACINTOSH.

THE CAPACITY OF THE MEDICAL PROFESSION IN AUSTRALIA TO ABSORB NEW MEMBERS.

SIR: In THE MEDICAL JOURNAL OF AUSTRALIA of October 17, 1953, there appears a very comprehensive and careful study by Dr. Poate of the medical needs of the Australian community and the availability of Australian graduates to supply them. Only one flaw can be detected—his estimate is based on clinical needs only, and no allowance has been made for the increase in "clerical medicine". This science, new to Australian civil practice and subsidized to the extent of at least 6s. per consultation by the Government (more for pensioners), is capable of vast expansion. The memory of the A46's lingers long after the proceeds of the TS4's have been returned to the treasury, and recent advances in paper warfare in Australia have proved that our post-war civil service cannot be considered decadent.

So long as the provision of social services remains a bait for voters, we can rely on the full support of all political parties and the applied ingenuity of all civil servants to develop "clerical medicine".

In other more socially advanced countries there seems to be plenty of work for all, but the clinical ability of their general practitioners is considerably lower than that of the Australian general practitioners; however, most clinically minded men can obtain salaried positions once they have higher degrees. Remuneration for clinical work is not high. In the hurly burly of the struggle for existence, clinical medicine must always give way to "clerical medicine".

No doubt a great deal of heat and energy will have to be expended in penmanship in our profession in future years, and intending students should be suitably warned and trained. A conservative source has estimated that if this heat and energy could be diverted to industrial needs, the Snowy River power project would be rendered superfluous.

Yours, etc.,

T. LOVEGROVE.

Wongan Hills,
Western Australia,
November 1, 1953.

FOLIC ACID AND REPRODUCTIVE EFFICIENCY.

SIR: We would like to thank W. J. Rawlings (1953) for his letter, as it gives us an opportunity to clear up some misapprehensions in regard to our papers on folic acid.

In this letter he states: "The difficulty is to find a numerical factor of that [folic acid] deficiency apart from the presumptive history." With this statement we are in whole-hearted agreement.

In our first paper (Lawson and Bolton, 1951) we stressed that our method of selection for folic acid treatment depended primarily on clinical grounds and that in the laboratory anisocytosis was considered to be quite equal in discriminatory value to the lymphocyte level.

If Dr. Rawlings wishes to take a single lymphocyte count as a standard of folic acid deficiency, it is reasonable to do so in a statistical investigation. We can speak with no certainty as to which lymphocyte level he should choose which will give him the greatest discrimination between groups. Our own figures indicate that 2000 lymphocytes per cubic millimetre could be a reasonable level to choose, but as it implies a lymphocytosis in normal pregnancy and as we have no certain knowledge of lymphocyte levels in normal pregnant women, we have preferred a level of 1500 per cubic millimetre partly because it is a quoted lower limit of normal and partly because it makes our test more stringent.

If, on the other hand, Dr. Rawlings desires to apply lymphocyte levels without reference to other factors in an individual case, and this seems possible from his letter, we hope that he has not been encouraged in this by anything that we have written.

In our first paper, we mentioned the inaccuracy of routine white cell and differential counts and gave support to this by quoting standard errors of our mean lymphocyte levels. From these it can be shown that the coefficient of variation for each of our three groups is in the region of 40%. Examining his counts, we find total lymphocytes and percentages are given to two figures. If we can conclude from this that white counts were obtained using a dilution of 1:20 with one pipette and counting two squares of one square millimetre in the chamber and also 100 cells in the differential count, it is possible to deduce a minimal coefficient of variation for his figures.

Using the formulæ found by Chamberlain and Turner (1952), this comes to 23·1%, and with a mean level of lymphocytes of 1645 gives an expected range at the 5% level of significance of 886 to 2406. It will be seen that this is not very different from his quoted ranges of 854 to 2848. (Even counting four squares for the leucocytes and 200 cells for the differential, the range is still 1051 to 2239.)

Quite apart from the inherent error in chamber and differential counts, we are well aware of the changes in lymphocyte level which occur as the result of stress and other factors and take these into account when assessing individual patients.

Why then do we use lymphocyte levels in our second paper (Lawson, DeGaris and Bolton, 1953)? Because it is the only numerical factor that we have to indicate possible folic acid deficiency, and therefore we must quote it to enable others to check our results.

In conclusion, we would like to emphasize that in dealing with an individual case the lymphocyte level is only part of a thorough survey including full physical examination, dietetic, past, family and environmental history undertaken before submitting a patient to the expense of folic acid therapy. That it is statistically able to select a group of patients with impaired reproductive efficiency is, we feel, a tribute to its value in obstetrics.

Yours, etc.,

D. F. LAWSON,
J. H. BOLTON,
C. N. DEGARIS.

Undated.

References.

RAWLINGS, W. J. (1953), M. J. AUSTRALIA, 2: 158.
CHAMBERLAIN, A. C., and TURNER, F. M. (1952), "Errors and Variations in White Cell Counts", *Biometrics*, 8: 55.
LAWSON, D. F., DEGARIS, C. N., and BOLTON, J. H. (1953), "Folic Acid and Reproductive Efficiency", M. J. AUSTRALIA, 1: 848.
LAWSON, D. F., and BOLTON, J. H. (1951), "Macrocytic Anæmia of Pregnancy", M. J. AUSTRALIA, 2: 669.

A REPORT ON AN INVESTIGATION OF A COUNTRY MIDWIFERY PRACTICE, WITH THE PRELIMINARY RESULTS OF 300 CASES FOLLOWING IMPROVED OBSTETRICAL CARE.

SIR: Dr. Cullen's article on a country midwifery practice in the journal of October 24 last was most interesting, but I felt that were doctors and statists to make a distinction between stillbirths and deadbirths their tables would be much more illuminating. In my student days a clear distinction was made between the two—the stillborn baby's heart was beating (in other words it was alive), whereas the deadborn baby was dead on delivery. Every obstetrician knows that many babies are stillborn in the sense given, and that the majority of them are saved by the proper restorative measures, and that many of them prove to be vigorous children. Moreover, we were taught that the difference between the two was of great legal importance in some cases, affecting inheritable rights.

I have looked up three dictionaries (including a medical one), and they all gave stillbirth as a deadbirth. On the other hand, old obstetric books distinguish between the stillborn and the dead baby, for example, Dakin (1897) and Johnstone (1918). Johnstone calls the lack of distinction an error of the legislators!

There is great clinical importance in recording whether the baby died during pregnancy but before labour, during labour or soon after labour, and whether it was dead or alive when born. Observation and recording of these points assist in determining the causes behind the loss of infants; these are sometimes mechanical, as too tight cord, or vaginismus hindering the birth of the shoulders or nurses holding the baby back (I was pleased to see that Dr. Cullen forbids this), which leads to premature inspiration.

Some time ago I analysed 106 forceps labours (107 children) occurring in albuminuric mothers; that is, the mother was ailing and the uterus inefficient. Twenty-three of these babies gasped when the head was born, and two cried audibly when head born; some of these babies required restorative measures, the most important of which was the removal by suction of mucus or liquor. Of the 107 children, 12 were deadborn and six stillborn, and 11 died later. Of the surviving children 65 required some help to breathe and cry, 29 of them a lot of help. In six of these children meconium was sucked out and in one blood. This is plain evidence of the risk and the frequency of premature inspiration, practically a drowning of the child. In several other cases Eve's rocker saved them when other measures failed. There seems to me no doubt that the state of health of the mother and the degree of efficiency of the uterus are largely responsible for the state of health and chances of survival of the infant. It is chiefly among toxic women who require forceps or who have premature labours that the deadbirths and stillbirths and neo-natal deaths occur, spoiling our statistics. The causes of the albuminurias and toxæmias of pregnancy and labour demand study and research, so that they may be prevented or at least controlled, thus saving many fine children.

Yours, etc.,

MARY C. DE GARIS.

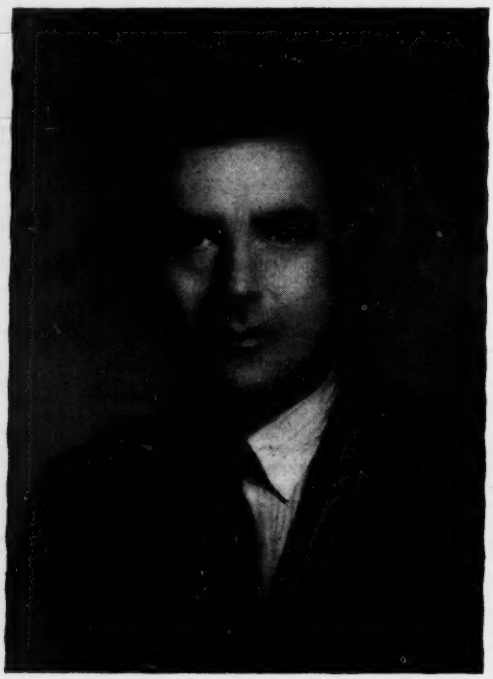
Geelong,
Victoria,
November 8, 1953.

Obituary.

JAMES HANNIBAL YOUNG.

We are indebted to Dr. J. Gordon Hislop for the following appreciation of the late Dr. James Hannibal Young.

The untimely passing of Dr. James Hannibal Young, at the age of forty-six years, will leave a gap in the ranks of the profession in Western Australia that will not easily be filled.



Young was educated at Guildford Grammar School in Western Australia and Saint Peter's College, Adelaide, qualifying at the University of Adelaide in 1929, gaining the Everard Scholarship, and obtaining the degree of M.D. ten years later, whilst in general practice in Wagin, Western Australia. He became a Member of The Royal Australasian College of Physicians in 1942 and gained his Fellowship in 1951.

The real work of his life did not become apparent until 1944, when, after he had come to the city, he began to exhibit a keen interest and insight into rheumatic disorders. Within two years he was contributing papers which were widely read, not only in Australia but abroad.

In 1948 he was invited to deliver papers in New Zealand. In 1949 came an invitation to attend the Congress of the American Rheumatism Association, of which he became a member in the following year. After this, he was invited to take part in the meeting of the Australasian Medical Congress (British Medical Association) at Brisbane.

There can be no doubt that Young contributed a great deal to our knowledge of disorders in the intervertebral disks. The interesting feature of his work is that it all evolved in the middle of a busy general practice, which, within a few years, was converted into a specialist practice, though still carried on from his suburban home.

Not only was he capable of making clear his views in writing, but his examination of a patient was a masterly exhibition of a confident approach to the disorder from which the patient was suffering, as well as a masterpiece of detailed observation and thinking of considerable rapidity. Within a very short space of time, Young had become accepted by the profession and the public as a master of his chosen craft.

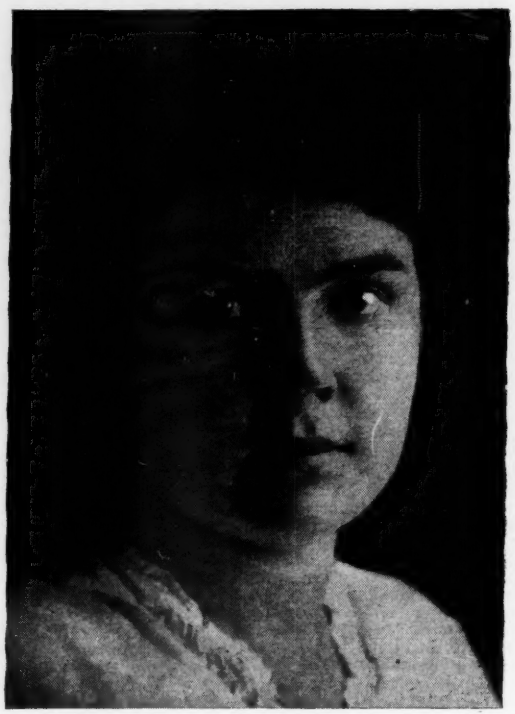
Medicine was not the only science in which he had become proficient. He was a keen amateur photographer of more than ordinary skill. His transparencies of Western Australian wildflowers must surely be the finest collection in existence. To obtain them, he travelled thousands of miles at appropriate times throughout the State. It is hoped that this work will be preserved.

But it was in the manner of his passing that his character was best displayed. Shaken for a day or two when a biopsy report of what was thought to be a hæmatoma returned a finding of squamous-celled carcinoma, he faced the inevitable with a courage that probably few of us possess. In the weary weeks of racking pain that followed, during which it slowly became obvious that treatment was proving ineffective, Jim calmly set about putting things into order for his family. Never did he utter one complaint concerning his fate, and, to the moment of his death, his active mind was attuned to the scientific aspect of his affliction.

There are many who will remember with gratitude the personality, the character, the skill and the artistry as well as the medical ability of Jim Young. Jim leaves a widow and a son and daughter.

JESSIE STRAHORN FREEMAN.

THE death of Dr. Jessie Freeman on August 25, 1953, should not be allowed to pass unnoticed. She was the first resident woman medical officer at Royal Prince Alfred Hospital and had been identified for many years with philanthropic organizations.



Jessie Aspinall was born in Forbes where her father, the late Reverend A. Ashworth Aspinall, M.A., was the first Presbyterian minister of the parish and built the first Presbyterian church. In Sydney Mr. Aspinall founded Scots College, Bellevue Hill, in 1893. He was Principal from 1893 to 1913. He had four sons and one daughter. Dr. Robert Aspinall, M.C., lost his life in the 1914-1918 war while serving with the Australian Army Medical Corps. Dr. Archie Aspinall and Dr. Eric Aspinall died within a few weeks of each other in 1945. Dr. A. Martel Aspinall, of Turramurra, is the surviving member of the family. All the brothers served in the Australian Army Medical Corps.

Jessie Aspinall was educated at the Presbyterian Ladies' College, Croydon, at Rivière College and at Kambala. In the senior examination she received the Gold Medal for the first place in the State and a Silver Medal for excellence in ancient history. She excelled in historical studies. Many school prizes testify to her all-round intellectual ability.

Jessie Aspinall graduated in medicine at the University of Sydney in December, 1905. She was then appointed resident medical officer at Prince Alfred Hospital. Her appointment as the first woman resident caused a sensation reflected in a vigorous newspaper controversy. A resident woman doctor was a startling innovation strenuously opposed in some quarters. Jessie Aspinall proved herself more than worthy of the post. Sir Charles Bickerton Blackburn commended her "exceptional tact in her dealings with both patients and nurses". The late Sinclair Gillies described her as "capable, painstaking, keen and reliable, and in addition a loyal and pleasant colleague". She was also described as "invariably cheerful and amiable and kind and attentive to her patients". The records show that her sound knowledge of medicine, her judgement and her tact won golden opinions. She had pioneered the way in Sydney for women doctors as hospital medical officers, opening a new chapter in Australian medical history. Subsequently she was the first woman resident medical officer in Tasmania when she was appointed to the Hobart General Hospital. Here she was described as a great favourite with the patients. She later served on the staff of the Women's Hospital, Crown Street, Sydney, as Medical Superintendent. Then she took rooms at Lyons Terrace near College and Liverpool Streets. This was an historic site in the annals of medical practice in Sydney, being at that time a locality for consultants. Jessie Aspinall moved to rooms in Wyoming, Macquarie Street, Sydney, where her reputation grew. She became quite a legend in the medical world in an era when women practitioners were still uncommon. Her undoubted charm, her professional skill, were often commented upon. Her determination and her fearlessness evoked general admiration. She had no qualms about entering unsavoury parts of the City of Sydney when duty called. Her sympathy and wise counsel were greatly prized.

In 1915 she married Ambrose William Freeman, B.A., B.E., M.I.M.E. After two periods in Malaya the family settled in Challis Avenue, Potts Point, at St. Killians, the original name of Scots College, and the home to which her father had retired in 1913. There were four children of the marriage, the Reverend A. R. A. Freeman, M.A. (Oxon.), W. A. A. Freeman, B.E., Mrs. A. W. Morton, B.A., Dip. Soc. Stud., and Dr. J. S. (Chantek) Freeman, now in London. The loss of Jessie Freeman's husband and his burial at sea after a relatively short period of married life threw a heavy responsibility upon her shoulders. She reared her young family with a vigour and a sense of stewardship which her children remember with deep gratitude.

Jessie Freeman was interested in many aspects of public life. She was a member for many years of the executive of the Victoria League, of the Appeals Committee of the Young Women's Christian Association, and of the National Council of Women. During the second World War she was the Vice-President of the Darlinghurst Branch of the Red Cross Society. In 1941 she made a gift of outstanding generosity when she presented to the Red Cross her home known as "Berida" at Bowral. This convalescent home, modern in every detail, has proved an undoubted boon to ex-servicemen and to their children. During her long life Jessie Freeman was a devout member of the Presbyterian Church. To her relatives and friends she has left cherished memories and a tradition which can be regarded with admiration and reverence.

Medical Practice.

POLICE OFFENCES AMENDMENT ACT, 1908, AS AMENDED.

THE following amendment to the Drug Regulations under the *Police Offences (Amendment) Act, 1908*, as amended, was published in the issue of the *New South Wales Government Gazette* of October 23, 1953. The amendment provides for the keeping of a new style register which is less complicated than the old one and enables a running record of the balance of a drug on hand to be shown after each transaction. The Under Secretary of the Chief Secretary's

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED OCTOBER 31, 1953.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	4(3)	2(1)	..	..	..	..	..	..	6
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	..	..	..	..	..	..	1	..	1
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	1	..	..	..	..	..	..	1
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	4(1)	..	..	..	..	..	..	..	4
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	2(1)	8(7)	9(5)	..	..	..	..	..	19
Diphtheria	4(1)	..	..	..	2(2)	..	..	..	6
Dysentery (Bacillary)	..	..	4(1)	..	1(1)	..	..	..	5
Encephalitis	1	..	..	..	..	..	..	..	1
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	..	14(5)	..	..	5(4)	..	..	..	19
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	..	..	..	..	..	..	..
Malaria	..	..	..	..	..	..	..	..	..
Meningococcal Infection	2(1)	2(2)	..	..	2(1)	2(1)	..	..	8
Ophthalmia	..	..	..	..	1	..	..	..	1
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	11(3)	..	..	5(4)	2(2)	..	..	..	18
Puerperal Fever	..	..	..	..	..	..	..	..	..
Rubella	..	22(9)	1(1)	..	100(91)	..	..	2	125
Salmonella Infection	..	..	..	..	..	..	..	..	..
Scarlet Fever	11(3)	26(20)	19(17)	2(2)	1(1)	..	..	..	59
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	1	2	..	1(1)	..	..	..	4
Trachoma	..	..	..	..	..	..	..	..	..
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	37(30)	9(4)	29(16)	11(8)	8(5)	3(1)	1	..	98
Typhoid Fever	1(1)	..	1	..	..	5	..	..	7
Typhus (Flea-, Mite- and Tick-borne)	..	..	2	..	..	..	..	..	2
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

Department states that stocks of the new register are now on hand at the Government Printing Office, but no adverse action will be taken against persons who continue to use the old type register until their present register has been completed.

[8464]

Chief Secretary's Department, Sydney, 23rd October, 1953.

His Excellency the Governor, with the advice of the Executive Council, has been pleased to amend in the manner set forth hereunder the Regulations under the Police Offences (Amendment) Act, 1908, as amended.

C. A. KELLY, Chief Secretary.

The Regulations under the Police Offences (Amendment) Act, 1908, as amended by subsequent Acts, are amended by *omitting* Schedule 5 and *inserting* in lieu thereof the following new Schedule:

SCHEDULE 5.

NEW SOUTH WALES.

Police Offences (Amendment) Act, 1908, as Amended by the Police Offences Amendment (Drugs) Act, 1927, and the Police Offences Amendment (Drugs) Act, 1934.

Drug

{One only, irrespective of strength, to page.} .....

Date.	Name and Address of Person or Firm to whom Dispenser sold or from whom Obtained.	In.	Out.	Balance.	Dispenser's Original Dispensing Number or Letter.	Name of Authority.	Actual Dispenser's or Administrator's Signature.

Australasian Medical Publishing Company, Limited.

ANNUAL MEETING.

THE annual meeting of the Australasian Medical Publishing Company, Limited, was held at The Printing House, Seamer Street, Glebe, on November 11, 1953, Dr. W. L. Calov in the chair.

Directors' Report.

The report of the directors of the company was as follows:

The directors submit their report for the twelve months ended June 30, 1953, together with the balance sheet as at June 30, 1953, and the profit and loss account for the twelve months ended June 30, 1953.

During the year contributions to THE MEDICAL JOURNAL OF AUSTRALIA covered a wide range of subjects, and there was an increase in the number of editorial pages. There was an improvement in the paper position during the year, and a more suitable paper was available for the journal.

The result of the year's production in the printing and publishing department was satisfactory, and arrangements have been made for the payment of debenture interest for the year ended June 30, 1953.

The company's reserves are used in the business, and we consider the state of the company's affairs is satisfactory.

Sir Henry S. Newland and Dr. F. W. Carter retire from office by rotation in accordance with the Articles of Association (Article 39). They are eligible and present themselves for reelection.

H. S. NEWLAND,
Chairman.

October 25, 1953.

Election of Directors.

Sir Henry S. Newland and Dr. F. W. Carter were reelected to the Board of Directors.

Deaths.

THE following deaths have been announced:

NEWALL.—Frederick Joseph Newall, on November 14, 1953, at Adelaide.

BLACKWOOD.—Frederick Martindale Blackwood, on November 20, 1953, at Killara, New South Wales.

Diary for the Month.

DEC. 7.—Victorian Branch, B.M.A.: Executive of Branch Council.
DEC. 8.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
DEC. 9.—Victorian Branch, B.M.A.: Branch Council Meeting.
DEC. 10.—New South Wales Branch, B.M.A.: Branch Meeting.
DEC. 15.—New South Wales Branch, B.M.A.: Ethics Committee.
DEC. 15.—New South Wales Branch, B.M.A.: Medical Politics Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federal Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

SUBSCRIPTION RATES.—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in the Commonwealth can become subscribers to the journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rate is £5 *per annum* within Australia and the British Commonwealth of Nations, and £6 10s. *per annum* within America and foreign countries, payable in advance.